Contents Page Section 4

Methods

Study Documentation

Recruitment @ UCLH

GYNAE-ONC CLINIC

CNS | Medical Consultants | Psychologists

3 Questions:

1) Are you having sexual problems?
2) Is this a problem for you?
3) Would you like some help?

Then, would you like to be part of the SAFFRON trial?

RAs

Inform face-to-face

24 hrs

Get Contact Details

24 hrs

Inform of study remotely

24 hrs

Informed Consent

Screening (FSFI ≤ 26?)

If yes

Baseline Trial Measures

RANDOMISATION

Stepped Care

ETAU

Self Help Booklet

Recruitment @ Bristol

GYNAE-ONC CLINIC

CNS | Medical Consultants | Psychologists

3 Questions:

1) Are you having sexual problems?
2) Is this a problem for you?
3) Would you like some help?

Then, would you like to be part of the SAFFRON trial?

RA's
(private room)

Get Contact Details
(inform later)

Inform face-to-face

24 hrs

24 hrs

Inform of study (phone/ post)

Book a future meeting

Informed Consent

Screening (FSFI ≤ 26?)

If yes

Baseline Trial Measures

RANDOMISATION

Stepped Care

ETAU

Self Help Booklet

Recruitment Script

"Hello, I'm Phil, and I'm one of the researchers on this new, exciting research project that is looking to help support women after they've had treatment for gynaecological cancers and are struggling with sexual or relationship problems, or ones to do with intimacy or self-esteem. So basically, we are testing a brand new way of delivering help and support called stepped care, and if you agree to take part you will helping us to improve patient care for women just like you, and to expand our knowledge of how best to treat women in this very sensitive area.

Please feel free to ask me questions at any time, and if I am giving you too much information or you don't understand anything then just let me know. You don't have to make any decision right now, I just want to give you an opportunity to fully consider whether this is something that you think you will be interest in participating in. We hope you will both gain something beneficial from it (as at the very least you will receive a booklet of information), but also you be contributing towards research and knowledge and understanding of cancer care.

Something I must tell you about is that this research project is randomised. This means that you have an equal chance of being allocated to either the group that receives the support or the group that receives treatment as usual. This is completely random but is required in order for us to know whether the new support we are testing and has any additional benefits comparative to the routine care you would have received anyway.

So what are the interventions? Well stepped care, which I mentioned earlier, is all about starting with a low level of support and then slowly building up that support if it is needed. Some people may only want some information about the problems they are experiencing or to know how common it is, whereas others may a higher intensity of support, and require a course of face to face therapy. We are looking to see if we can use this idea of increasing levels of support on women who've had gynaecological cancer and are struggling with the sexual side of their recovery.

There are 3 different levels of support available within this study, and depending on your wishes and your scores on some questionnaires you may be offered all three of these interventions. The first level is just a self-help booklet for you to take home and read, and some advice on things you could try or do that may be helpful. The second level is delivered by a clinical nurse specialist, and involves you meeting privately with them and having a conversation with the problems you are facing and getting the chance to really ask the questions you may have been afraid to ask, or just having someone to listen. For this Level 2 support there will be at least 3 sessions for you to attend, and some homework for you to do. And then, after that, if you still feel that you need additional support then we will arrange for you to have a full course of what is called interpersonal therapy. Now this is 16 sessions of therapy with a clinical psychologist and really allows you to address the sexual problems you have been facing and explore some psychological solutions with a professional.

I've got a sheet here that has all this information written down for you, and its important that you go home and read this and maybe have a discussion within your family or a friend, or whoever, and really think about your decision to take part. But we hope that if you do take part that it will be really beneficial to you. And if you do feel you want to take part now but then change your mind at some point in the future then you can withdraw at any time, without having to give a reason. And you can always ring me, my number is on the sheet, to discuss any of these things. It's all completely in confidence. We really understand that this is a sensitive issue but research shows us that many women have these problems with relationships, or intimacy or sex after cancer but are too

embarrassed or think it's not important enough to seek help for it. So we're trying to change that and find out how we can best support women through this journey after their treatment.

So do you have any questions for me? Is there anything you would like to go over again?

If you do agree to participate, and after we have contacted you to let you know which group you have been randomly allocated to then its really important that you don't describe or discuss any of the information you receive with other women who may be in the study. Obviously you can tell people that you are part of the study, and discuss the content with friends and family but as much as possible we want to keep the two groups within the study separate so that we can be sure that the treatment is working.

Further, if you feel that this study is something that you would be interested in in the future, but maybe now is not the right time, then you can contact me anytime between now and July 2016 to have another discussion about the study and maybe begin treatment.

Recruitment Pathway via Units

Royal Free | Whittington | North-Middlesex | Harlow | Barnet

Local CNS

3 Questions:

1) Are you having sexual problems?
2) Is this a problem for you?
3) Would you like some help?

Receive study information

Then, would you like to be part of the SAFFRON trial?

Referral to Clinical Psychologist @ UCLH

Allocation meeting (Administrator/ Clin Psych)

CDR Updated

RA's informed

7 days

Patient Contacted & informed

PIS/ Consent mailed to patient

Clinical Appointment

Brief assessment with Clinical Psychologist (SG)

RA's inform patient

Informed Consent

Screening (FSFI ≤ 26?)

If yes

Baseline Trial Measures

RANDOMISATION

Stepped Care

ETAU

Self Help Booklet

4.5 SAFFRON level 2 training

Powerpoint presentation for CNSs

SAFFRON level 2 training

Sue Gessler

UCL/UCLH

SAFFRON

SAFFRON: Developing a *S*tepped *A*pproach to improving sexual *F*unction a*F*te*R* treatment f*O*r gy*N*aecological cancer

Plan of day

- Introductions
- Summary of SAFFRON history
- SAFFRON structure of study
- The three levels of intervention
- Background to the level 2 intervention
- Session 1
- Session 2
- Session 3

Background

- Political
  - historically psycho-oncology funding via Cancer Research UK
  - 2008-9 National Cancer Survivorship Initiative- CRUK focus moves to translational and clinical research, specifically excluding all psychology intervention studies and quality of life (prevention studies only)
  - Macmillan take QoL role but ‘don’t fund research’

- Scientific
  - often psycho-oncology functions in a vacuum
  - not linked to theory
  - evidence base for interventions often derived outside cancer
  - most funded studies are US (NIH, University funds) and target breast cancer patients
  - psycho-oncology studies don't attract general funding because not seen as developing theory – just a special application

NIHR commissioned call

- Committee generates issues that require research to answer a specific question that will benefit patients in the NHS
- Take suggestions from public, clinicians and scientists
- Specific call in 2010 for feasibility study for interventions to improve sexual functioning in women affected by gynaecological cancer
- Not funded: re advertised in 2011

Call fitted Women's Cancer UCL

- Institute for Women's Health (NHS/UCL)
- NHS department of gynae-oncology with consultant clinical psychologist
- academic link with senior research fellow nurse
- need to integrate research with clinical structures
- opportunity to work with UCLp

What's the problem?

- cancer patients in general report sexual difficulties post treatment
- gynaecological cancer covers ovary, cervix, womb and vulva: treated with surgery +/- radiation +/- chemotherapy, damaging nerves, tissue, hormones
- sexual difficulty rates from 40% to 100%
- lack of desire, dyspareunia, vaginal dryness, orgasmic difficulty, pain, fatigue, change in bowel activity (+/- stomas), urinary symptoms – leakage, depression, anxiety, fear

- little relationship between extent of interventions and sexual function measures(Hazewinkel et al 2012, Carpenter et al 2009)
- major issues of mood disorders (23% prevalence according to Thompson and Shear 1998)
- very low likelihood of patient discussing with physician (62% of 221 patients reported sex never addressed by physician Lindau et al 2007)

What helps?

- discussion with physician
- CNS input
- 2 Cochrane reviews found only evidence for topical oestrogen and creams, vaginal dilators and lubricants
- no strong evidence for any psychosexual interventions

Current best practice

- PLISSIT model adopted from USA sexual therapy in general (non cancer)
- P = permission
- LI= limited information
- SS= specific suggestions
- IT= intensive therapy (ie by specialist practitioner)

Difficulties with the study as commissioned

- diverse population- multiple ages, tumour sites, types of treatment, prognosis, pre- or post –menopause
- premorbid sexual state difficult to ascertain
- relationships pre diagnosis may vary widely
- typical response post trauma to assign blame to the trauma – perhaps sex was bad before?

Vision for study

- harnessing power of UCL – psychological therapies development unit key part of UCLp
- envision intervention as entirely psychological, patient and symptom driven
- ignore medicalising assumptions that specific causes will have similar sexual effects (cf trauma)

Principles of study and call

- address mood issues specifically
- also needs not to pathologise normal response to cancer and its treatment
- reach maximum number of women
- maximise basic conversations around having a problem, normalising and giving basic information
- retain more complex input for women not helped by entry level help

Stepped intervention modelled on IAPT

- IAPT =Increasing Access to Psychological Therapies
- Lord Layard – national roll-out
- GP screen for entry PHQ9, GAD7
- begin with bibliotherapy, self help leaflets
- if not effective, low-intensity workers with specific structured interventions
- if not effective, stepped up to high intensity (clinical psychologist) for full intervention

team

- Prof Peter Fonagy
- Prof Alessandra Lemma
- Prof Steve Pilling
- Prof Michael King
- Louise Jones
- Anne Lanceley
- Karen Summerville
- Adeola Olaitan
- Susan Dunning (pt advocate)
- Julie Barber
- Rachael Hunter
- Sue Gessler

Aims and objectives

- 1. To establish whether women treated for gynaecological cancer with moderate to severe sexual dysfunction are willing to participate within a randomised trial model and adhere to treatment
- 2. To indicate likely rates of recruitment to a future evaluation of SAFFRON intervention
- 3. To pilot a stepped care psychosexual intervention (SAFFRON) on the IAPT model and compare its effect on sexual dysfunction to treatment as usual
- 4. To establish whether the SAFFRON intervention is acceptable to patients
- 5. To establish whether SAFFRON is deliverable by a gynae-oncology cancer centre multi-disciplinary team
- 6. To inform the effect size, sample calculation and outcome measures for use in a larger definitive trial

Research Questions

- 1. Will women agree to be randomised to a sexuality intervention?
- 2. Are different tumour sites, treatments, cancer stages at approach associated with different rates of uptake of therapy/intervention or recruitment to trial?
- 3. Is the stepped care system operable within the NHS system as it stands?
- 4. What is the likely effect of the three levels of intervention on sexual function, mood and self esteem as measured by standard measures?
- 5. What is the rate of attrition from each treatment modality?

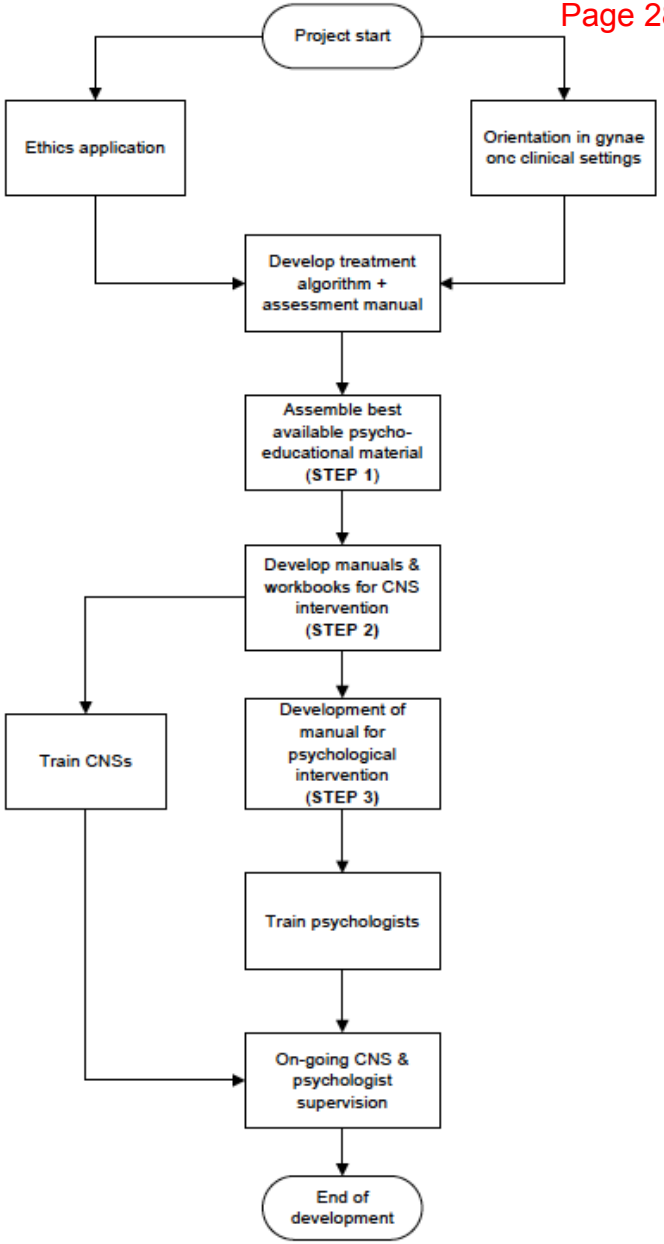
Design and theoretical/conceptual framework

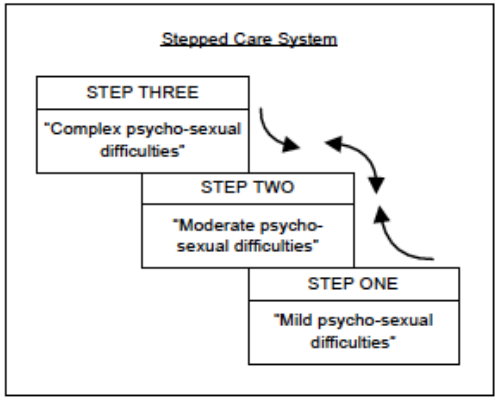
- feasibility study: Two arm, parallel group, randomized controlled trial.
- HTA call required a feasibility study; a new intervention requires a pilot RCT.

SAFFRON part 1- development

- (1) An integrated, stepped care system for the assessment and routine outcome monitoring of women with psychosexual problems (including mood and self-esteem);
- (2) A series of treatment manuals detailing the interventions provided at each step;
- (3) A brief training programme for clinical nurse specialists (CNS) and psychological therapists providing the interventions.

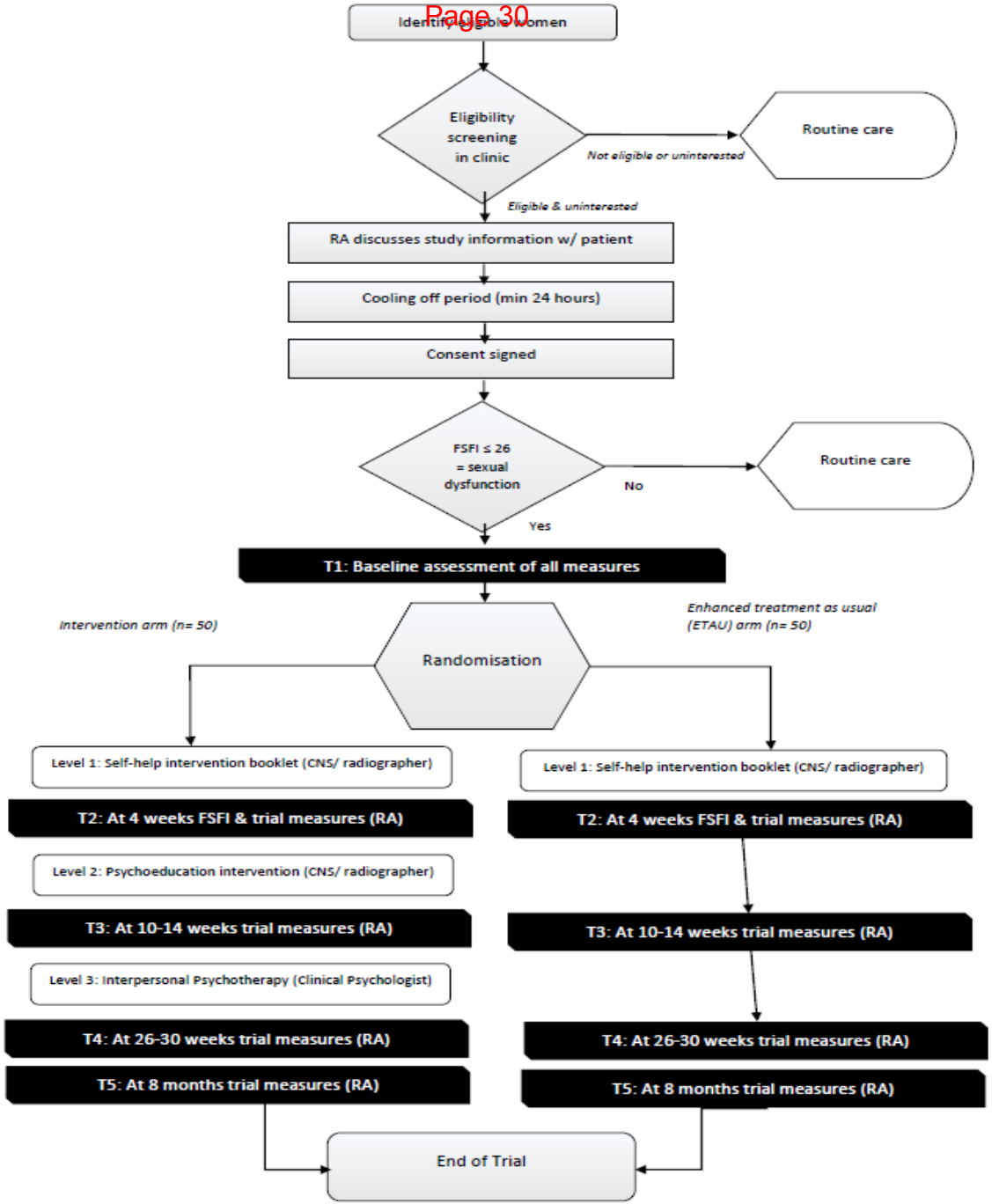
SAFFRON PART 1: Development (1 - 6 months)





SAFFRON part 2

- an exploratory randomised trial to assess
- (1) referral rates, acceptance of randomisation and attrition
- (2) uptake of and attrition from the interventions offered;
- (3) acceptability and feasibility of the trial outcome measures;
- (4) feasibility and experience of establishing a stepped system for the delivery of the intervention;
- (5) feasibility of the CNS/radiographer/psychologist training;
- (6) potential effect sizes of the interventions;
- (7) qualitative data on experiences of women in the trial(8) estimates of the potential magnitude of the effect of the intervention, with confidence intervals to determine whether these are consistent with clinically important effects and
- (9) estimates required to inform the sample size calculation for a large RCT(10) feasibility of collecting cost and quality of life information for a cost-utility analysis of stepped care compared to TAU in a full trial.
- Findings will provide estimates of sample size calculation and treatment effects with confidence intervals to inform the need to conduct a definitive trial.


Identify eligible women
Eligibility screening in clinic
Not eligible or uninterested
Routine care
Eligible & uninterested
RA discusses study information w/ patient
Cooling off period (min 24 hours)
Consent signed
FSFI ≤ 26 = sexual dysfunction
No
Routine care
Yes
T1: Baseline assessment of all measures
Intervention arm (n= 50)
Randomisation
Enhanced treatment as usual (ETAU) arm (n= 50)
Level 1: Self-help intervention booklet (CNS/ radiographer)
Level 1: Self-help intervention booklet (CNS/ radiographer)
T2: At 4 weeks FSFI & trial measures (RA)
T2: At 4 weeks FSFI & trial measures (RA)
Level 2: Psychoeducation intervention (CNS/ radiographer)
T3: At 10-14 weeks trial measures (RA)
T3: At 10-14 weeks trial measures (RA)
Level 3: Interpersonal Psychotherapy (Clinical Psychologist)
T4: At 26-30 weeks trial measures (RA)
T4: At 26-30 weeks trial measures (RA)
T5: At 8 months trial measures (RA)
T5: At 8 months trial measures (RA)
End of Trial

Target population - inclusion

- Women over 18 (with partners at their choice) treated for any gynaecological malignancy with surgery and/or chemotherapy and/or radiation
- 3 months minimum post end of treatment
- with sexual function difficulties identified by initial screen (3 clinical questions)
- any sexual orientation

Exclusions

- Poor English
- Current drug or alcohol abuse
- Current sexual therapy or psychotherapy

interventions

- Control arm – enhanced treatment as usual ie treatment as usual plus level 1 booklet (psycho-education booklet for trial)
- TAU: CNS advice on the use of dilators, lubricants and topical creams
- Intervention arm-
- Level 1–All women with a psychosexual problem who request help and consent to entry to the trial receive level 1 psycho-education booklet
- trial entry will not preclude CNS advice as usual in parallel

Level 2

- – All women who have not responded to step 1 as assessed on NATSAL-SF and self report
- Women will receive an enhanced psychosexual intervention based on the work of Brotto et al (2008) with IAPT input (Pilling/Gessler).
- Delivered in 3 core sessions (face to face or telephone) with one to two follow up sessions at 12 weeks after the first sessionThe interventions will be delivered by CNS or gynae-trained radiographer.

Level 3

- All women with a psychosexual problem who have not responded to step 2 and request further help.
- Level 3 is be 16 session high intensity intervention NICE recommended treatment for depression(Interpersonal therapy adapted by Alessandra Lemma for gynae-oncology and sexual difficulties) delivered by a clinical psychologist.

Baseline Assessment – all measures below (T1)	4 Weeks (T2)	3 Months (T3)	6 Months (T4)	8 Months (T5)
Demographics, personal history				
Diagnosis, stage, treatment				
FSFI	X	X	X	X
EuroQol 5D (EQ-5D-5L)	X	X	X	X
Client services receipt inventory (CSRI) (short form)			X	X
PHQ-9	X	X	X	X
GAD-7	X	X	X	X
Sexual QOL				X

Sample size

- 100 – 50 in each arm
- Assume 50% consent (80% in depression treatment trials is usual)
- Recruiting at Bristol and UCLH in parallel

Success criteria to move to main trial

- set as:
- consent rate of at least 40%
- minimum of 30% in the intervention group moving up at least 1 step on the intervention
- at least 70% of randomised subjects having a useable (non missing) score for total FSFI (our primary outcome) at 12 months follow-up
- And use feasibility data to provide estimate of standard deviation of FSFI score required for sample size calculation of main trial.

Plan of investigation and timetable

Project milestones
0-6 months -orientation, ethics, research governance, develop intervention and assessment algorithm, write manuals and materials, train CNSs and psychologist
7-15 months –recruitment and intervention
16-27 months – follow-up, qualitative interviews with women and staff, begin qualitative analysis 28-30 months – complete analysis and write

SAFFRON Timetable

Months	0-3	4-6	7-9	10-12	13-15	16-18	19-21	22-24	25-27	28-30
Project tasks										
Ethics Application										
Orientation in gynaecological OPD										
Develop treatment algorithm & manual										
Assemble best available psycho-education										
Develop manuals & workbooks for CNS										
Develop manual for psychological intervention										
Train psychologists										
Train CNS										
Ongoing CNS & psychologist supervision										
Recruitment			Pilot							
Intervention			Pilot							
Follow-up										
Patient interviews										
Health care professional interviews										
Analysis - qualitative										
Analysis - quantitative										
Write up										
Dissemination										

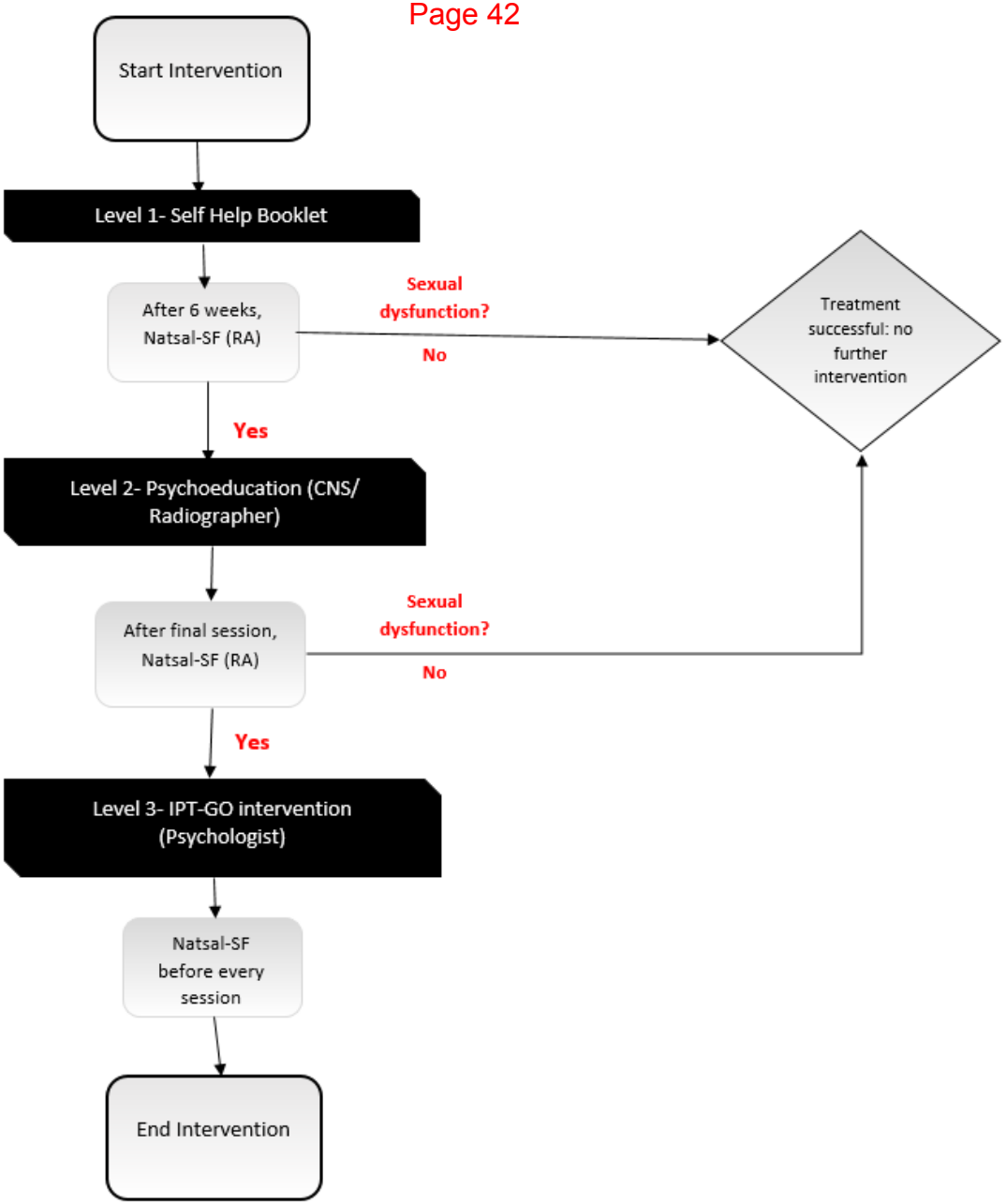
Coffee

Coming to a psychological intervention as a non psychologist

- Your background
- Any anxieties?
- What you bring

A feasibility study

- Your input critical to understanding the training
- Your needs as you develop through delivering the intervention
- Keeping notes (today, through the study)
- Model: ‘Supervising to competence’
- Fidelity to model – measuring not *your* skill but the effectiveness of the SAFFRON training and supervision


Start Intervention
Level 1- Self Help Booklet
After 6 weeks, Natsal-SF (RA)
Sexual dysfunction?
No
Yes
Treatment successful: no further intervention
Level 2- Psychoeducation (CNS/ Radiographer)
After final session, Natsal-SF (RA)
Sexual dysfunction?
No
Yes
Level 3- IPT-GO intervention (Psychologist)
Natsal-SF before every session
End Intervention

Why this intervention?

- Only evidence based intervention found in gynae cancer
- Psychological – mix of psycho-education and therapeutic intervention
- 3 sessions
- Brotto L, Heiman J, Goff B, Greer B, Lentz G, Swisher E, et al. A psychoeducational intervention for sexual dysfunction in women with gynecologic cancer. Arch Sex Behav 2008;37(2):317–29.

Session 1

- brief, intensive assessment of the woman's sexuality, concentrating on sexual arousal
- explore sexual beliefs that influence the woman's current sexual experience
- develop shared language with woman

Review manual for session 1

- How to do a behavioural analysis
- Role play key areas
- Your comments and key issues

Assessment of sexual issues

- end of session 1 – ask woman to rate 3 most problematic areas for her
- drop-down list plus free writing
- to rate 0-100 each session as guide to how therapy is progressing

Session 2

- provide feedback from the assessment of her current sexuality conducted in session one
- discuss role beliefs have in the woman's sexual experience, to encourage her to consider other ways of looking at such beliefs
- review the homework exercises on relationship and body image
- provide psychoeducation on factors implicated in enhancing sexual arousal
- discuss normative age-related and relationship-related changes in sexual desire.

Session 3

- review the homework exercises on focusing, self-observation, and touch as adapted for her particular post-treatment state
- build upon earlier discussions on the potential role of her intimate relationship in her current experience of sexuality if appropriate
- provide the woman with additional education on factors implicated in enhancing sexual arousal.

Next steps

- R&D
- Recruitment
- Phil MacNamee and Becky Anderson- how can they support you?
- Launching SAFFRON on both sites
- Where and when will you see your patients?
- Supervision slots
- Taping sessions

4.6 SAFFRON - Brief PowerPoint presentation for study sites and staff groups

SAFFRON

Developing a Stepped Approach to improving sexual Function aFteR treatment fOr gyNaecological cancer

BRIEF: What is SAFFRON?

- SAFFRON is a feasibility RCT testing the implementation of a stepped care intervention for women who received treatment for gynaecological cancer and are presenting with psycho-sexual difficulties.

Background

- Occurrence of sexual difficulties high with 40-100% – NIHR called for trial submissions.
- Low likelihood of patients discussing sexual problems with physician (Lindau et al. 2007 found 62% of N=221 reported that sexual functioning was not discussed in consultation).
- Post-operative symptoms for women with gynaecological cancer can be profound and vary (lack of desire, dyspareunia, vaginal dryness, orgasmic difficulty, pain, fatigue, change in bowel activity (+/-stomas), urinary symptoms – leakage, depression, anxiety, fear).
- High prevalence of mood disorders (23% according to Thompson & Shear 1998).
- Evidence base for gynae-oncology psycho-sexual interventions not sufficient and existing interventions are not linked to theory.
- NIHR call for feasibility study

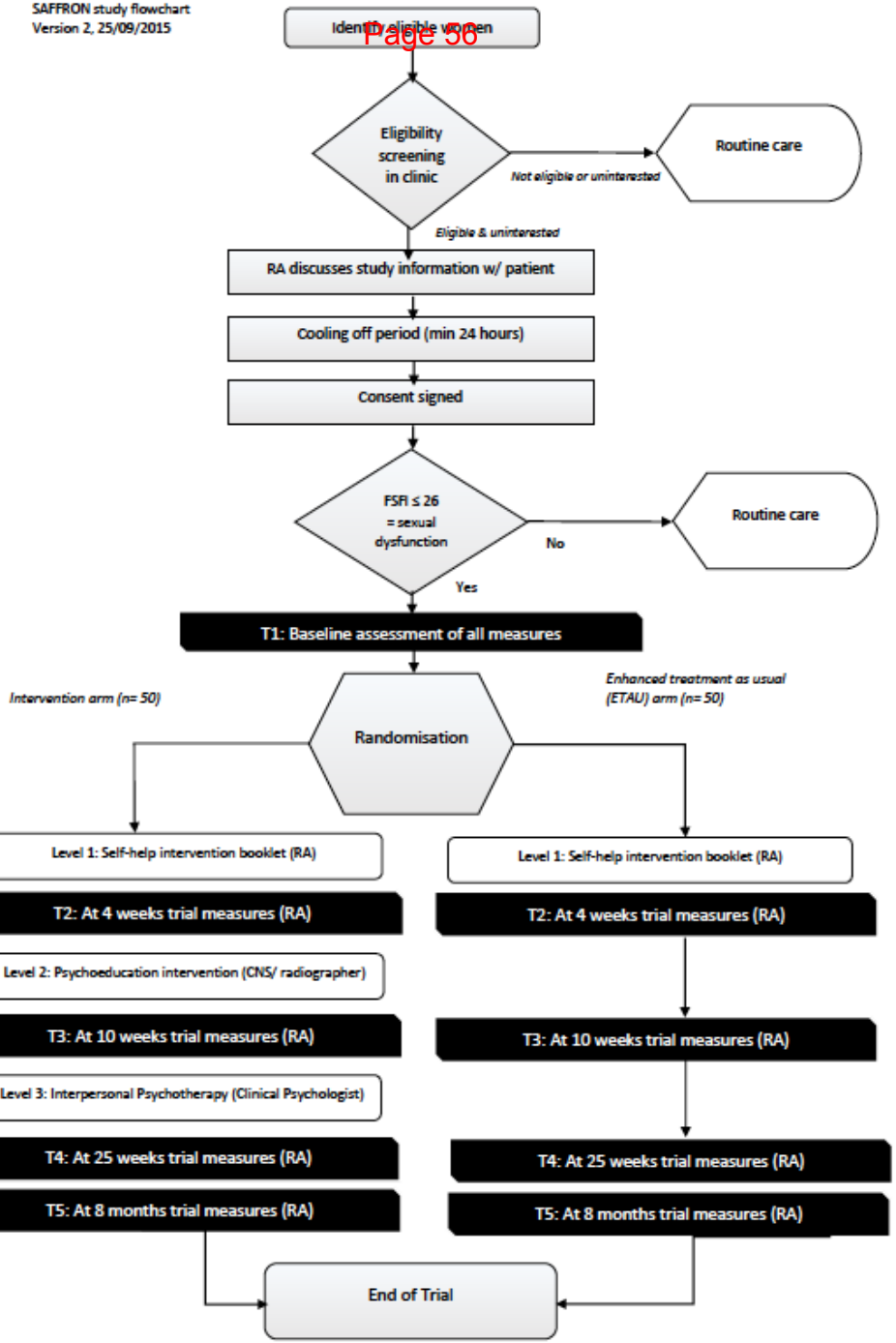
Aims and objectives

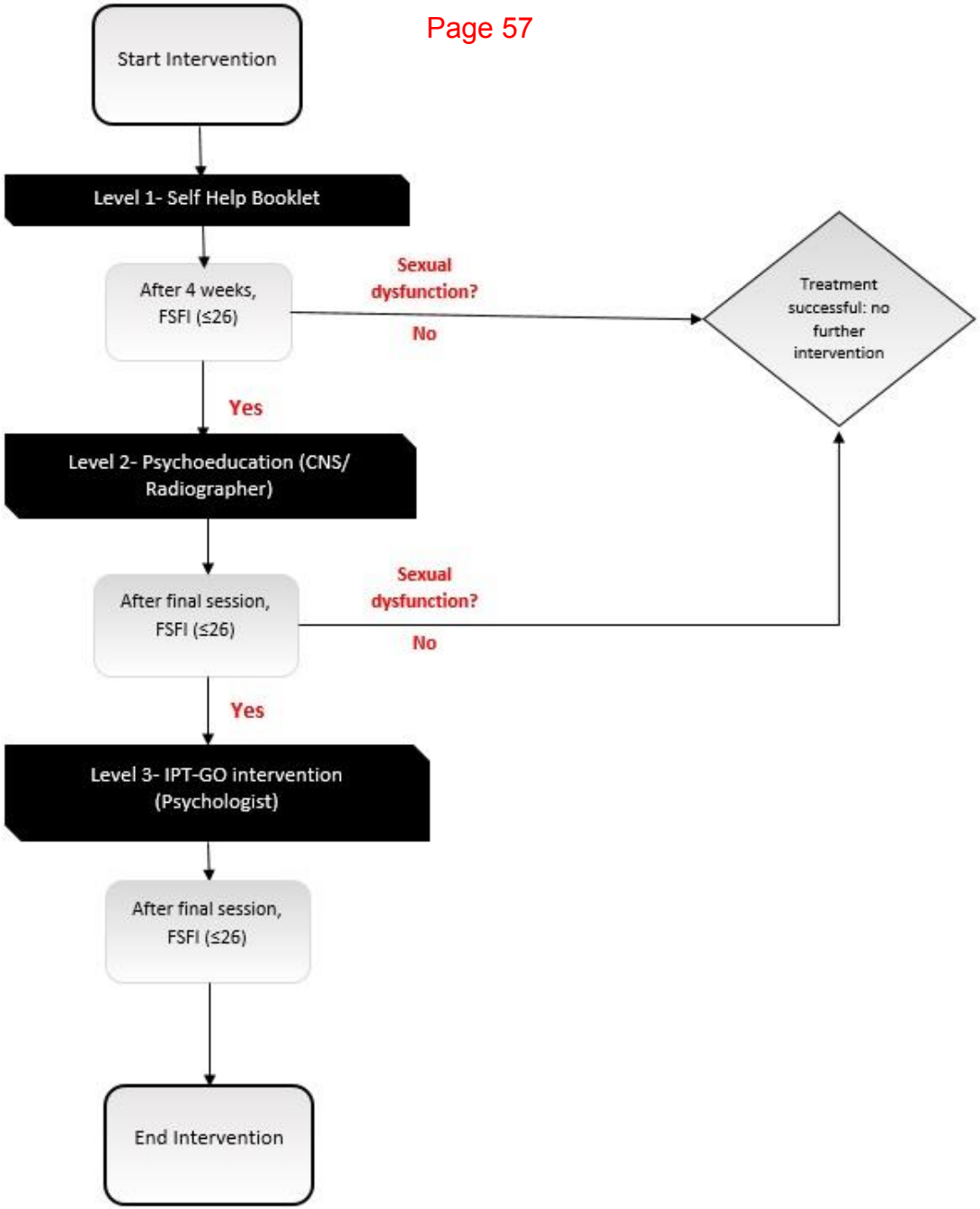
1. To establish whether ***women*** treated for gynaecological cancer with ***moderate to severe sexual dysfunction*** are ***willing to participate*** within a randomised trial model and adhere to treatment.
2. To indicate likely ***rates of recruitment*** to a future evaluation of SAFFRON intervention.
3. To ***pilot a stepped care psychosexual intervention*** (SAFFRON) on the IAPT model and compare its effect on sexual dysfunction to
4. treatment as usual.
5. To establish whether the SAFFRON ***intervention is acceptable*** to patients.
6. To establish whether SAFFRON is ***deliverable*** by a GN cancer centre multi-disciplinary team.
7. To inform the ***effect size***, ***sample calculation*** and ***outcome measures*** for use in a larger definitive trial.

Design

- Feasibility study: Two arm, parallel group, randomized controlled trial.
- HTA call required a feasibility study; a new intervention requires a pilot RCT.
- Sample size: N = 100 (50 in each arm); assumption that 50% of approached patiens consent to take part

SAFFRON study flowchart
Version 2, 25/09/2015



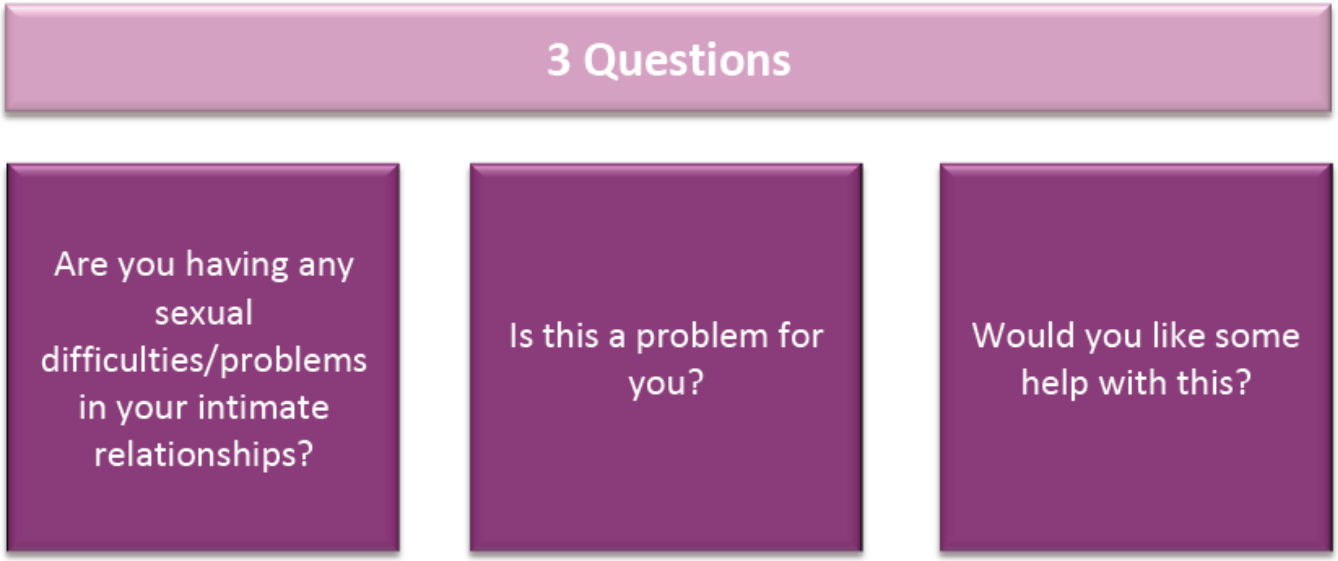

Start Intervention
Level 1- Self Help Booklet
After 4 weeks, FSFI (≤26)
Sexual dysfunction?
No
Treatment successful: no further intervention
Yes
Level 2- Psychoeducation (CNS/ Radiographer)
After final session, FSFI (≤26)
Sexual dysfunction?
No
Yes
Level 3- IPT-GO intervention (Psychologist)
After final session, FSFI (≤26)
End Intervention

Exclusion / inclusion criteria

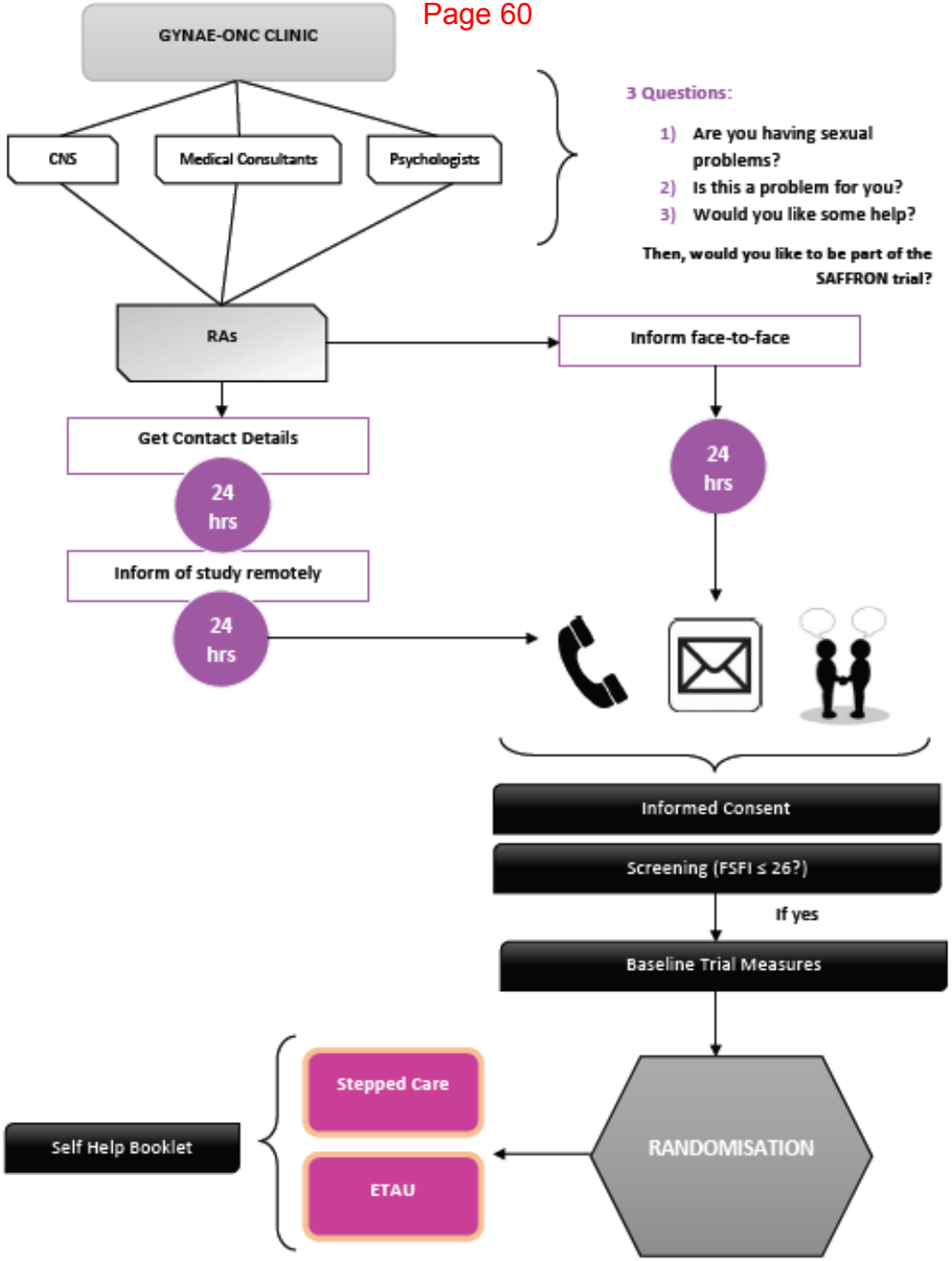
- Women over 18 (with partners of their choice) treated for any gynaecological malignancy with surgery and / or chemotherapy and / or radiation.
- Three months minimum post end of treatment.
- With sexual function difficulties identified by initial screening questions.
- Any sexual orientation.
- Patients with poor English, current drug / alcohol abuse, and current sexual therapy or psychotherapy are excluded.

Identification of participants

- Two sites (UCLH & Bristol) will identify potentially eligible patients by asking 3 questions at follow-up:



Recruitment @ UCLH



How you can help with recruitment.

1. Awareness of general inclusion criteria.
2. Identifying eligible women by asking the 3 questions.
3. Referring patients to UCH team by contacting admin or research assistant team.

Acknowledgments

- Prof Peter Fonagy, Prof Alessandra Lemma, Prof Steve Pilling, Prof Michael King, Louise Jones, Anne Lanceley, Karen Summerville, Adeola Olaitan, Susan Dunning (patient advocate), Julie Barber, Rachael Hunter
- …

Additional slides

Rationale for study

- ***Culture change*** – addressing the lack of communication between health professionals and patient in respect of sexual functioning after cancer treatment.
- Need for addressing ***mood difficulties*** in women.
- Equally, ***normalising*** and not pathologising response to illness and its treatment.
- Improving ***access to care*** and enhancing ***communication*** about psycho-sexual problems in a gynae-oncology health care context.
- Tailoring interventions to the specific needs of this population, i.e. ***stepped care approach*** – retain more complex support for women not helped by entry level input.

Research questions

1. Will ***women agree to be randomised*** to a sexuality intervention?
2. Are ***different*** tumour ***sites***, treatments, cancer stages at approach associated with ***different rates of uptake*** of therapy/intervention or recruitment to trial?
3. Is the ***stepped care system operable*** within the ***NHS*** system as it stands?
4. What is the likely ***effect*** of the three levels of intervention ***on sexual function***, mood and self esteem as measured by standard measures?
5. What is the ***rate of attrition*** from each treatment modality?

Current best practice

- No unified, evidence-based approach to treating psycho-sexual problems in women with gynaecological cancer.
- PLISSIT model adopted form US sexual therapy (not cancer specific) → P = permission, LI = limited information, SS = specific suggestions, IT = intensive therapy

Visions for study

- Harnessing power of UCL – psychological therapies development unit key part of UCLp.
- Envision intervention as entirely psychological, patient and symptom driven.
- Ignore medicalising assumptions that specific causes will have similar sexual effects (cf trauma).

Limitations of study as commissioned

- Diverse population- multiple ages, tumour sites, types of treatment, prognosis, pre- or post –menopause.
- Premorbid sexual state difficult to ascertain.
- Relationships pre diagnosis may vary widely.
- Typical response post trauma to assign blame to the trauma – perhaps sex was bad before?

SAFFRON – Part 1 (Development)

1. An integrated, stepped care system for the assessment and routine outcome monitoring of women with psychosexual problems (including mood and self-esteem).
2. A series of treatment manuals detailing the interventions provided at each step.
3. A brief training programme for clinical nurse specialists (CNS) and psychological therapists providing the interventions.

SAFFRON – Part 2 (Implementation)

An exploratory randomised trial to assess

1. Referral rates, acceptance of randomisation and attrition.
2. Uptake of and attrition from the interventions offered.
3. Acceptability and feasibility of the trial outcome measures.
4. Feasibility and experience of establishing a stepped system for the delivery of the intervention.
5. Feasibility of the CNS/radiographer/psychologist training.
6. Potential effect sizes of the interventions.
7. Qualitative data on experiences of women in the trial(8) estimates of the potential magnitude of the effect of the intervention, with confidence intervals to determine whether these are consistent with clinically important effects.
8. Estimates required to inform the sample size calculation for a large RCT(10) feasibility of collecting cost and quality of life information for a cost-utility analysis of stepped care compared to TAU in a full trial.

- Findings will provide estimates of sample size calculation and treatment effects with confidence intervals to inform the need to conduct a definitive trial.

Success criteria to move to main trial

- Consent rate of at least 40%.
- At least 70% of randomised subjects having a useable (non missing) score for total FSFI (our primary outcome) at 8 months follow-up.
- Use feasibility data to provide estimate of standard deviation of FSFI score required for sample size calculation of main trial.

Who is involved?

- Two NHS sites: UCLH & Bristol
- Team:
  - Prof Peter Fonagy, Prof Alessandra Lemma, Prof Steve Pilling, Prof Michael King, Louise Jones, Anne Lanceley, Karen Summerville, Adeola Olaitan, Susan Dunning (pt advocate), Julie Barber, Rachael Hunter
  - Sue Gessler (CI), Phil Mcnamee (RA), Becky Anderson (RA)

Part II.
How SAFFRON will be implemented

Study flow chart

Intervention

Level 1

- Targets mild psycho-sexual difficulties
- Received by all consenting participants (self-help booklet)

Level 2

- Targets moderate psycho-sexual difficulties
- Received by women who did not respond to level 1 as measured with NATSAL-SF
- Enhanced psycho-sexual intervention delivered in 3 core sessions by CNS / radiographer

Level 3

- Targets complex psycho-sexual difficulties
- Received by women who did not respond to step 2 and request further help
- High intensity 16-session intervention delivered by clinical psychologist

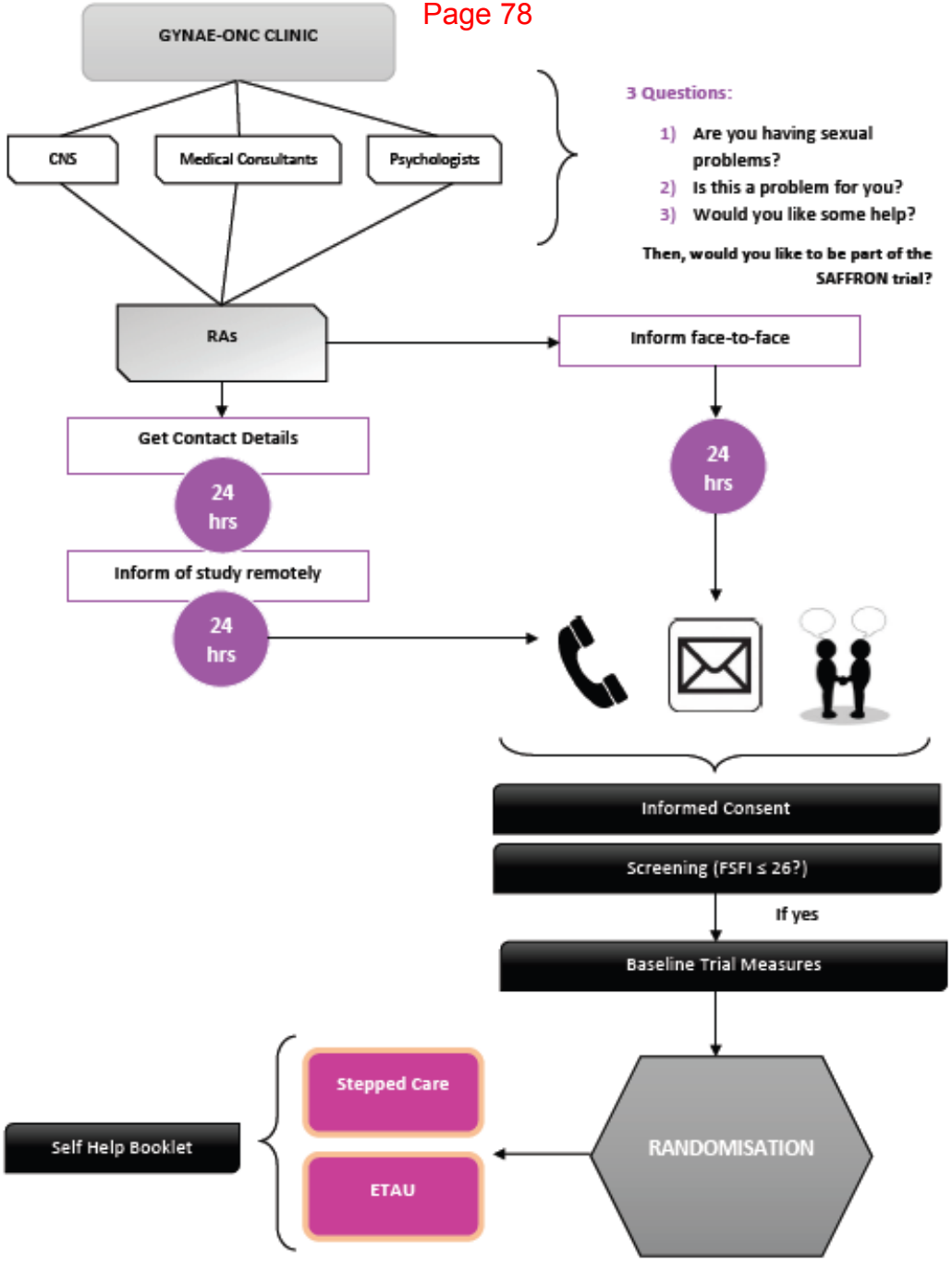
Assessment measures

Name of outcome measure	Baseline (T1)	4 Weeks (T2)	3 Months (T3)	6 Months (T4)	8 Months (T5)
Demographics, personal history	X				
Diagnosis, stage, treatment	X				
FSFI	X			X	X
SQOL	X	X	X	X	X
EuroQol 5D (EQ-5D-5L)	X	X	X	X	X
Client services receipt inventory (CSRI) (short form)	X			X	X
PHQ-9	X	X	X	X	X
GAD-7	X	X	X	X	X
Preference Measure	X		X	X	X
Satisfaction Measure (intervention arm only)				X	X

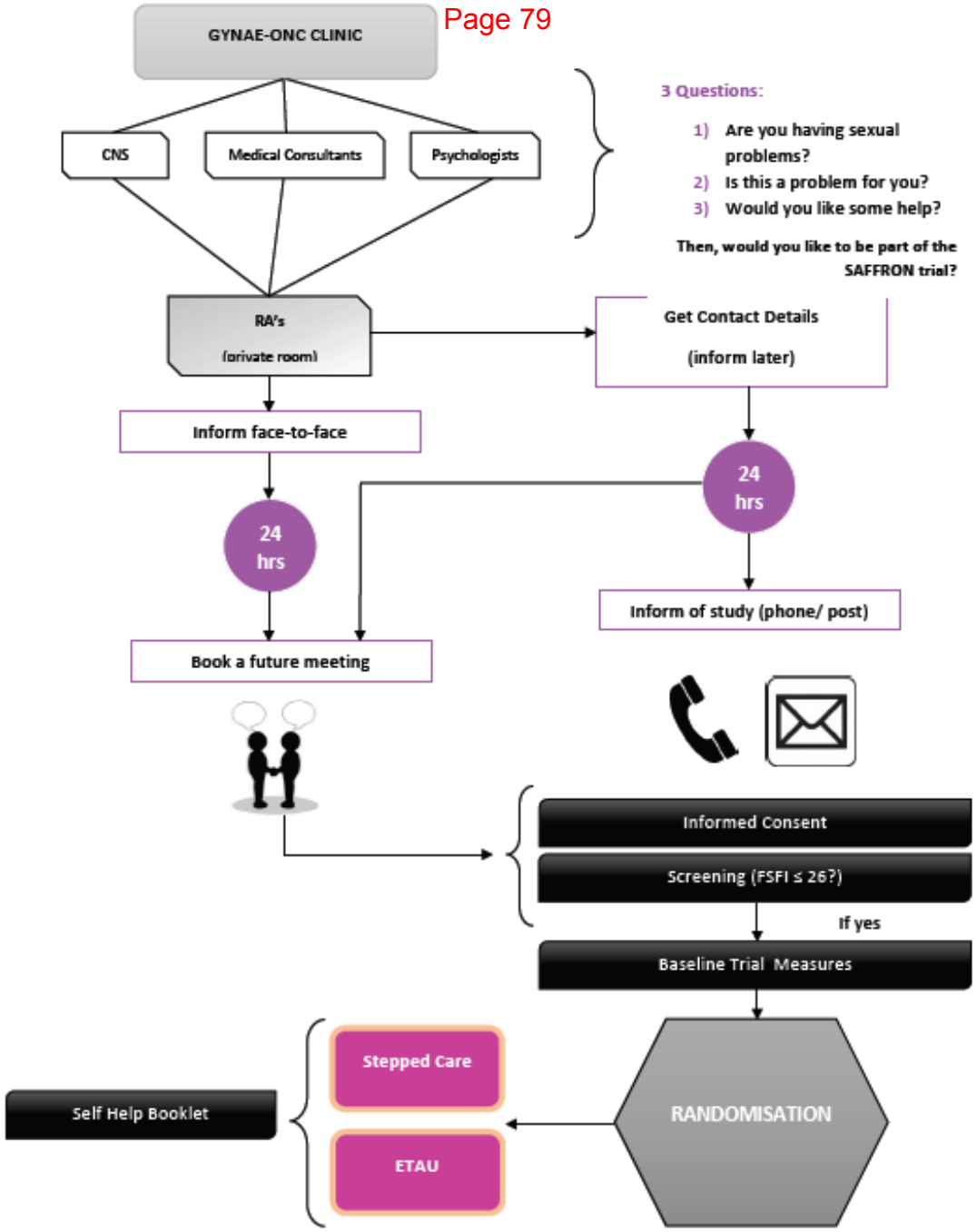
Recruitment strategy

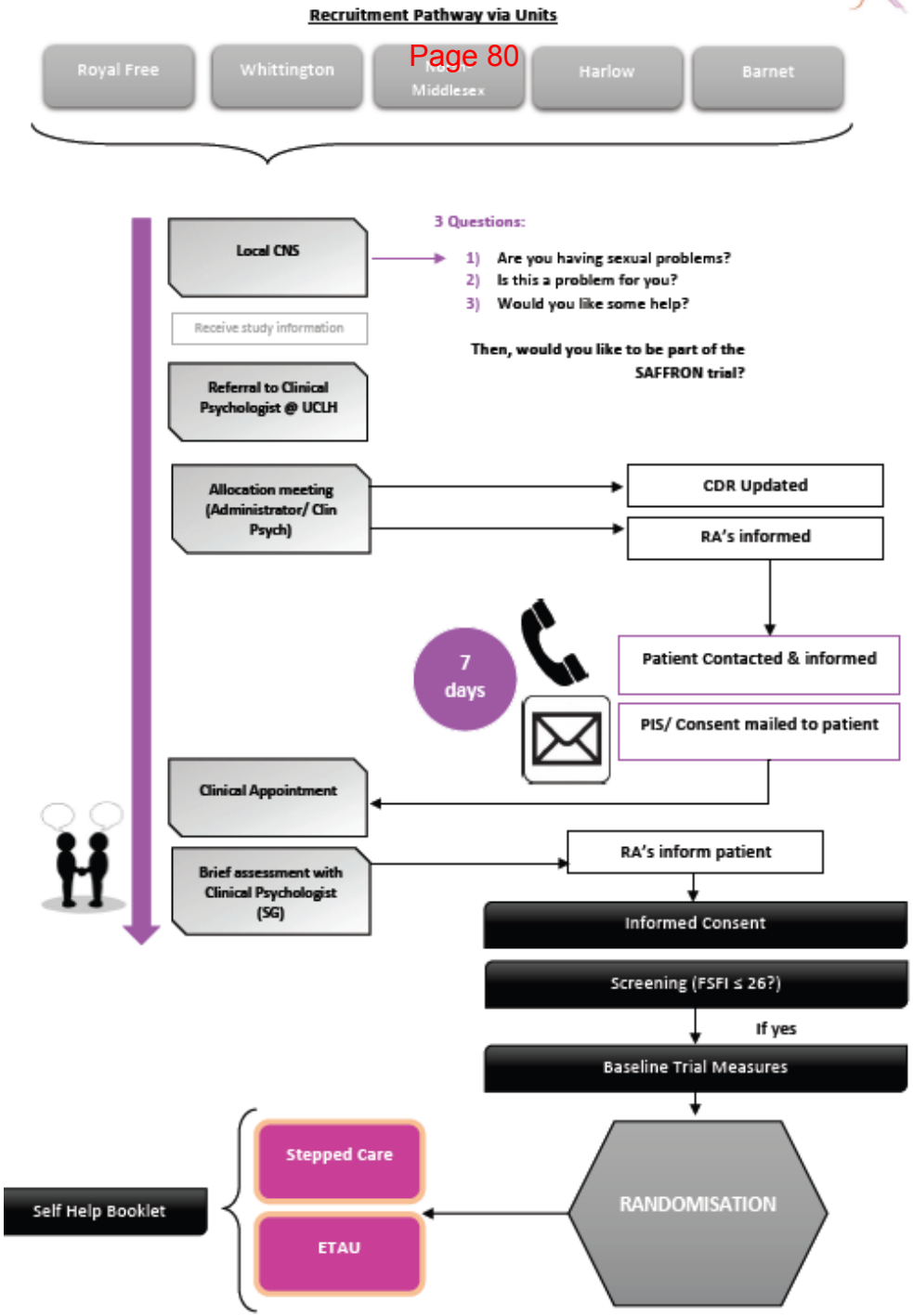
- Flow charts for recruitment sites

Recruitment @ UCLH



Recruitment @ Bristol

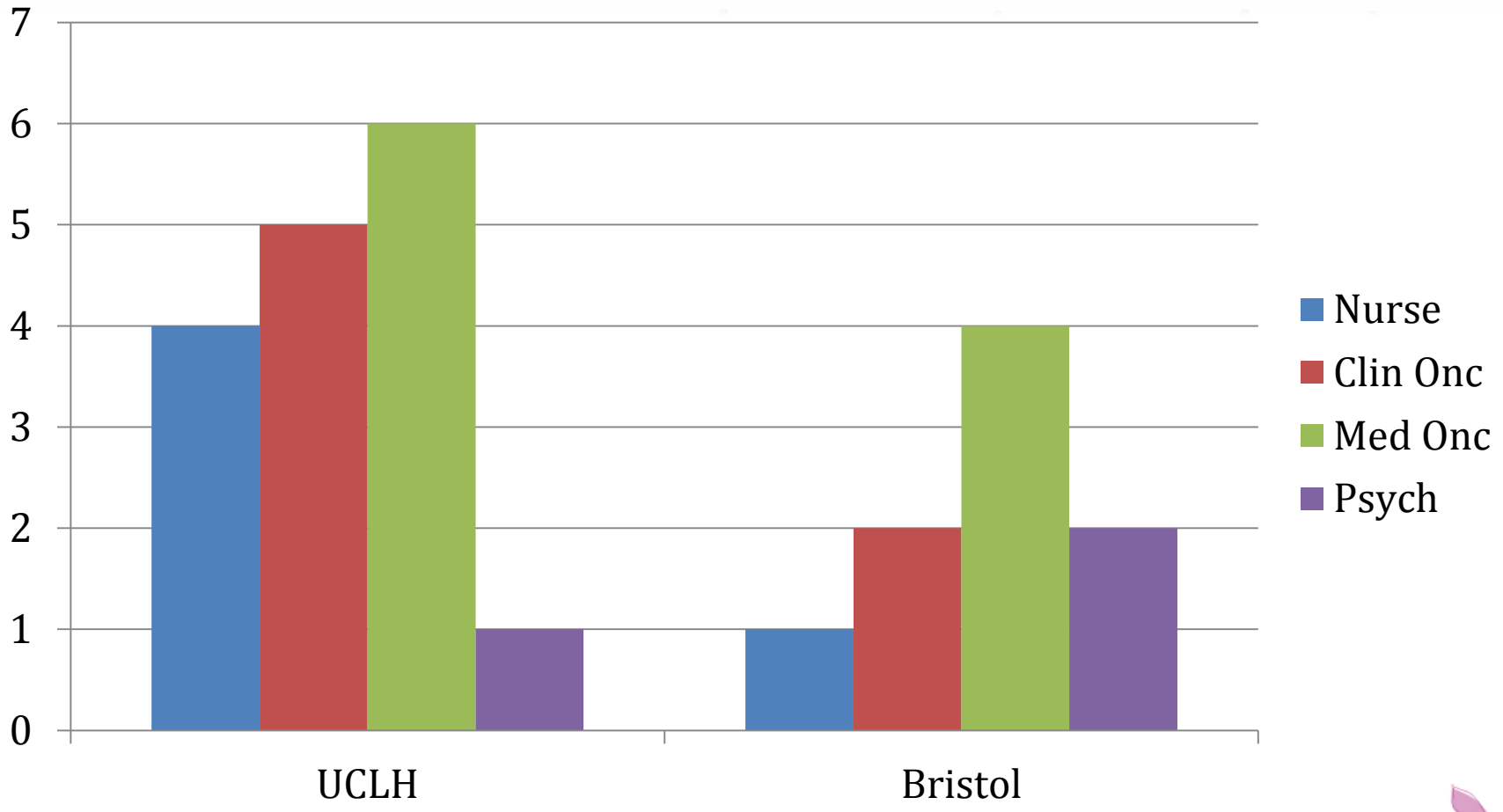



Recruitment Pathway via Units
Royal Free
Whittington
Middlesex
Harlow
Barnet
Local CNS
3 Questions:
1) Are you having sexual problems?
2) Is this a problem for you?
3) Would you like some help?
Then, would you like to be part of the SAFFRON trial?
Receive study information
Referral to Clinical Psychologist @ UCLH
Allocation meeting (Administrator/ Clin Psych)
CDR Updated
RA's informed
7 days
Patient Contacted & informed
PIS/ Consent mailed to patient
Clinical Appointment
Brief assessment with Clinical Psychologist (SG)
RA's inform patient
Informed Consent
Screening (FSFI ≤ 26?)
If yes
Baseline Trial Measures
RANDOMISATION
Stepped Care
ETAU
Self Help Booklet

Obstacles to recruitment and how to overcome them

- Psycho-social study in medical setting; busy environment; time restricted
  - Integrating and being part of the team
  - De-burdening clinical staff, i.e. completing assessment, consenting patients, providing a treatment pathway, providing training for clinical staff
- Patients' attendance / compliance to research protocol
  - Cultivating relationships with participants
- Talking about sex – culture change in follow up
  - Normalising

Recruitment update (example)



Future projects

- Supervising to competence model (PhD project)

University College London Hospitals NHS
NHS Foundation Trust

4.7 SAFFRON GP Letter

Department of Women's Cancer
Gynaecological Cancer Research Unit
University College London
1st Floor Maple House
149 Tottenham Court Road
London, W1T 7NF

Address: …….

Date: ……..

Title of Project: Developing a Stepped Approach to Improving Sexual Function after Gynaecological Cancer: a feasibility study. (SAFFRON)

Dear Doctor,

Re: ……

Address: ……

……

This letter is to inform you that your patient has given her written consent to participate in the above study.

Researchers and clinicians at University College London and University College London Hospital (UCLH) and Bristol Cancer Centre are conducting the study. The study is a two arm, parallel group pilot randomised controlled trial in women with sexual difficulties following gynaecological cancer treatment. The aims of the NIHR HTA funded study are to:

* Improve sexual functioning in women treated for gynaecological cancer while taking into account associated issues of mood
* Measure the overall cost-effectiveness to the public sector of providing treatments, compared to costs of subsequent use of health and social services.
* Assess the feasibility of conducting a full scale investigation of a stepped therapy approach and indicate the potential benefits to the patients, their partners, and to the NHS generally.

The 30 month pilot study will recruit 100 women from two cancer centres in London and Bristol. Women with any gynaecological cancer at any stage are eligible on the principle that sexual difficulty is the problem we are treating, not the cancer of origin.

The study will use and adapt existing evidence based therapies for improving sexual function after cancer treatment and develop a model for delivering these in the NHS setting. The model of 'stepped care' is adapted from that used nationally and successfully in the Increasing Access to Psychological Therapies programme, where mood disorders are picked up in general practice and managed at a range of levels, from self -help through 'low intensity' interventions up to 'high intensity' interventions. Assessment at beginning and throughout all treatments allows for 'stepping up', i.e. calibrating the type of help a woman receives according to her need and her response to the treatment already given.

The study will develop and evaluate the 'stepped' system of interventions together with an algorithm for assigning treatment level. Stepped care will use elements of the best available evidence, adapting existing interventions to help women recover their sexual feelings and activity. The initial assessment will determine which step is suitable initially, and women can be progressed from one therapy to another as appropriate using a newly developed algorithm based on sessional scores on a validated outcome measure. Stepped care starts with simple methods moving on to new talking treatments delivered by a psychologist for more complex cases, based on theories of how we treat loss and depression.

Ongoing clinical assessment will be vital for the success of the stepped care model. We will deliver training and supervision to enhance the skills needed by the Clinical Nursing Specialist. An important part of this study will be characterising the range of women and their willingness to participate in psychosexual help. Your patient may be asked to take part in a one-to-one interview to inform the level of input required for any subsequent large Randomised Control Trial.

Women consenting to take part in the study will randomly receive one of two options:

* Enhanced treatment as usual
* Stepped care.

Your patient Ms/Mrs XX…. has been randomised to [insert either standard treatment as usual or stepped care]

[Then either insert)

You patient will receive the same treatment as she would have received were there no study. She will get help via her doctor, nurse or other sources such as the Macmillan information services. This may involve psycho-educational booklets, advice leaflets on psychosexual problems; advice on the use of dilators, lubricants and topical creams and face to face or telephone advice and support from her clinical nurse specialist. In addition, she will receive a specially prepared psycho-educational self-help booklet which has been prepared for the SAFFRON study. We will give women in both groups this booklet and this is why we call it Enhanced treatment as usual as we have added in something that she would not usually get.

or

Stepped care involves a package of treatments adapted from existing well established treatments for women with sexual difficulties after cancer.

These will be delivered by the clinical team who would look after your patient normally and will include: targeted self-help books, medicinal treatments and counselling sessions given by a specially prepared clinical nurse specialist (CNS) or possibly a psychologist depending on our assessment of what is happening for her. She will have regular clinical assessments and treatments based on these e.g. between 2-5 20-30 minute counselling sessions either face-to-face or over the telephone or if experiencing more severe difficulties up to 16 therapy sessions of 50 minutes delivered by a psychologist. If the assessments show there is little improvement in your patient's sexual recovery she would be 'stepped up' to receive other treatments.

Your patient will participate 'on study' for 12 months.

It is acknowledged that a study about sexual difficulties in women with gynaecological cancer is sensitive. The study team are experienced in these areas and able to identify distress. If your patient is unduly distressed by her participation, with her permission, you would be informed. Ms/Mrs X is of course free to withdraw from the study at any time without giving a reason and this would not affect the standard of care she receives.

We will use validated rating scales for rating sexual function, as well as assessing how illness and treatment affect mood and self-esteem, choosing scales which are as brief as possible for participants, in order to minimise drop out. It will take approximately 15 minutes for your patient to complete the patient reported outcome questionnaires for the study at baseline, 6 weeks, then 3, 6, and 12 months.

Should you have any concerns or questions regarding this study, please contact:

Dr……. Tel:

Yours sincerely,

Dr. (Insert name of local PI)

SAFFRON Informed Consent Working Practice Document

- Patients should have at least 24 hours from discussing the study with the RA and receiving the Participant Information Sheet (PIS) before being asked to consent to taking part in the study

- Where possible, informed consent should be taken at an appointment at the clinic. However home visits can be arranged and if an appointment cannot be made, consent can be taken over the phone/ post (see below)

- Confirm with the patient that she has read the PIS and ask if she has any questions

- Explain what will happen if the patient decides to take part in the study and ensure she understands everything from the initial discussion. Remember it may have been a number of months since the initial discussion took place

- Explain that once consent has been taken, we will need to complete a questionnaire to ensure that the study is suitable for her and she can take part

- Give the patient another chance to ask any questions

- Go through each point on the consent form with the patient. When she is happy with each point, ask her to initial in the boxes and print, sign and date 2 copies of the form in black ink

- The RA should then do the same and give one copy back to the patient

- The RA should later make 2 more copies of the consent form and put the original in the Investigator Site File, one copy in medical notes, and one copy in TMF

- Complete T1 measures (see T1 SOP)

Consent over phone/ post

- When the patient cannot attend an appointment, consent may be taken over the phone/ post

- Before the phone call, post the consent form, all T1 measures and a self-addressed envelope. When arranging the phone call, tell the patient not to complete any of the measures, but that she can have a look through to get an idea of what the study involves

- Go through the information above with the patient

- Ask the patient to initial in the boxes and print, sign and date the consent form and return it to UCL

- Arrange a time to call for T1 measures

- When you receive signed consent form, counter-sign it and make 3 copies (put the original in the Investigator Site File, one copy in medical notes, and one copy in TMF)

- Send the last copy back to the patient along with randomisation allocation once this has been done

After Recruitment

- Once written informed consent has been received then the individual must be logged on the NIHR portfolio, NETSCC Management Information System (MIS), and the EDGE system (UH Bristol patients only).

SAFFRON Working Practice Document: Initial discussion of the trial

Setting

- Ensure that clinicians know which room you are in so that they can send patients straight through to you (wait outside room so that the clinicians don't forget to send patients to you)

- If you do not have access to a room try to find a quiet area if the patient is comfortable with this. Otherwise offer the patient tea, water etc. If it seems like it will be a long wait give her the PIS to read through

- The patient may not have time to talk to you, or you may not be able to find a private space, in which case she can complete a contact details form and this discussion can be done over the phone

- If the patient has been referred through the units, this conversation will always be over the phone. Ensure that you call at least 24 hours before the appointment with SG (appointments are likely to be booked well in advance so should be possible to make the call at least 7 days before)

Discussion of trial

- Check eligibility (can ask all questions except FSFI)

- If the patient is not eligible, give her the self-help booklet and refer to routine care. Explain why she is not eligible to take part and stress that there are a wide range of treatments available and that by receiving the booklet she will be getting the same intervention as 50% of the women eligible for the study. Inform clinical team of outcome

- Go through recruitment script

End of Discussion

- Explain that the patient doesn't have to decide straight away, she can let us know any time up until June 2016 if she wants to take part. This will be the final day of recruitment and if she has not contacted us by then she cannot take part as the study will have finished

- Give the patient the PIS and tell her that if she has any questions whilst reading it to call the researcher (details on the PIS)

- Agree on a date for the researcher to call the patient to see if she has decided to take part and book consent appointment

- If the patient has been referred through the units, post/ email PIS. She will already have an appointment, so no need to call again, but ensure she knows that she can cancel the appointment if she decides not to take part

SAFFRON Stepping-up Working Practice Document

- At the end of Level 1 and Level 2 interventions, all women in the intervention arm should be assessed to see whether it is appropriate to increase the intensity of the intervention they are receiving
- The end of Level 1 is defined as 4 weeks after receiving the self-help booklet
- The CNS/ Radiographer will inform the RA when the final session of the Level 2 intervention is so that the researcher can meet with the patient after the appointment to go through the assessment
- At both timepoints, complete the FSFI with the patient (if she is uncomfortable doing this with you verbally, she can complete it herself independently)
- If the patient scores >26 explain that she has shown improvements and so will not be stepped-up to the next level of the intervention. If she feels that she needs more help, direct her to her CNS who can refer to relevant services. Tell the patient that we will still be contacting her to go through questionnaires for the study

Assessment Following Level 1 Intervention

- If the patient scores ≤26 following Level 1, explain that she can be stepped-up to the next level of the intervention.
- Explain that this will involve seeing a CNS/ radiographer for 3 counselling sessions, ideally face-to-face
- Remind the patient that these sessions will be recorded
- Ask whether she is happy to continue with the intervention, or whether she would like some time to think about it first. If the patient would like some time, arrange a time to call and go through the following information
- Tell the patient that she will be assessed again following this intervention
- Give the patient an appointment to see the CNS/ radiographer (most likely to be Fridays for Vikky at UCLH or Mondays for Pauline at Bristol)
- Inform CNS/ radiographer of appointment and give patient details including FSFI overview
- Inform Level 3 clinician that they may receive a referral in around 6-10 weeks
- Send a text reminder to the patient before their appointment

Assessment Following Level 2 Intervention

- If the patient scores ≤26 following Level 2, explain that she can be stepped-up to the next level of the intervention.
- Explain that this will involve seeing a clinical psychologist for 16 therapy sessions of 50 minutes
- Give patient IPT info sheet
- Remind the patient that these sessions will be recorded
- Arrange a time to call and check whether she would like to continue with the intervention and go through the following information
- Tell the patient that this is the final stage of the intervention
- Tell the patient that the clinical psychologist/ administrator will be in touch to make an appointment
- Inform clinical psychologist and give patient details including FSFI overview

SAFFRON T1 Working Practice Document

Screening

Once informed consent has been taken, complete the FSFI with the patient and calculate score using excel spreadsheet or score sheet (this will be in the same session as consent if done face-to-face, otherwise will be a separate phone call)

- Complete eligibility form (this should already have been checked during the initial discussion, but reconfirm answers)

- If the patient scores >26 or does not meet other inclusion/ exclusion criteria, give her the self-help booklet and refer to routine care. Explain why she is not eligible to take part and stress that there are a wide range of treatments available and that by receiving the booklet she will be getting the same intervention as 50% of the women eligible for the study. Inform clinical team of outcome

- If the patient scores ≤26 and meets other inclusion/ exclusion criteria, explain that she is eligible to take part and that we will need to go through a number of questionnaires. After the appointment inform the patient's consultant that the patient is eligible using template letter

Baseline Assessment of all Measures

- Complete the following questionnaires with the patient:
  - Demographics and Medical History
  - SQOL-F
  - EQ-5D-5L
  - PHQ-9
  - GAD-7
  - Health Care Resource Use
  - Preference measure

- If the patient is uncomfortable going through these questions with you verbally they can complete them independently

- Explain that we will be asking these questions at various points over the course of the study to see if anything has changed

Randomisation

- Explain that later in the day/ the following day the RA will use a computer to decide at random which group the patient will be in and that this is 50/50

- Make sure that the patient has the researcher's contact details and tell her that whichever group she is assigned to, we will call her to inform her of the outcome

- When back in the office, input patient details and questionnaires into SAFFRON database and randomise patient as per database instructions

- This will create participant ID. Add this to all source data collection forms and update the excel database

- Call the patient to inform her of the outcome. Explain that we will send her a letter with this information in more detail, and that if she likes we can call her once she has received this to discuss it further

- Send randomisation allocation letter to the patient, along with the counter-signed consent form and self-help booklet

- Send letter to inform the GP of the allocation

- If the patient is randomised to the intervention group, contact the Level 2 clinician to inform them that they may receive a referral in 4 weeks

Phone T1 Session

- Once consent has been received, call the patient to go through questionnaires following the instructions above

- When completing the questionnaires, the patient's versions are for her reference only and data should be collected over the phone

- If a patient is feeling fatigued, she can post the questionnaires back instead, however the FSFI and inclusion/ exclusion criteria must be done on the phone to ensure eligibility

SAFFRON T2, T3, T4 & T5 Working Practice Document

Call patient a week before measures are due. Explain that we need to go through some questions to see how she is feeling. Either arrange an appointment or tell her that you will post the questionnaires and call in a week to go through them

Questionnaires

- Complete the questionnaires indicated below:

Name of Outcome Measure	4 Weeks T2	14 weeks T3	25 weeks T4	8 months T5
SQOL	X	X	X	X
EQ-5D-5L	X	X	X	X
PHQ-9	X	X	X	X
GAD-7	X	X	X	X
Preference Measure		X	X	X
Health Care Resource Use			X	X
FSFI			X	X
Satisfaction Measure (intervention arm only)			X	X

Stepping-up

- Depending on the timing of individual patients' interventions, it may be appropriate to also carry out the assessment for stepping-up to the next level of the intervention in the same appointment. See separate SOP for stepping-up procedure.

T5

- At T5 explain that this is the end of the intervention study and thank the patient for her time
- If the patient feels she still needs more help, direct her to her CNS who can refer to relevant services
- Tell the patient that we will be interviewing some participants about their experiences of taking part and ask if this is something she would be interested in. Explain that we may not need to talk to her but that we will be in touch
- Send end of trial letter to the patient

Phone T2-5 Sessions

- Arrange a time for the call and post patient questionnaires

- Follow instructions above

- When completing the questionnaires, the patient's versions are for her reference only and data should be collected over the phone unless feeling fatigued by questionnaires, in which case they can post the questionnaires back instead