Process Evaluation

Analysis Plan

FINAL Version 1.0

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Glossary of abbreviations

DMEC Data Monitoring and Ethics Committee
HTA Health Technology Assessment
NIHR National Institute for Health Research
PMG Project Management Group
TOPSY **T**reatment **O**f **P**rolapse with **S**elf-care pessar**Y**
TSC Trial Steering Committee
RCT Randomised Controlled Trial

1. Introduction

The NIHR HTA commissioning brief asked for an internal pilot study "to demonstrate the ability to recruit and randomise, and participants' adherence to allocated treatment, with clear stop/go criteria to the main trial". This document sets out how the process evaluation data will be collected, analysed and reported. Quantitative data where referred to will be analysed in line with the conventions laid out in the main trial Statistical Analysis Plan (SAP) except where stated otherwise.

TOPSY includes a nested process evaluation which runs alongside the main RCT. The process evaluation will collect and analyse qualitative and quantitative data about recruitment, intervention fidelity, participants' experiences of participating in the trial and adherence to trial protocols and group assignment. Findings will be reported to PMG, TSC, DMEC and HTA.

2. Our definition of 'on treatment'

For women self-managing their pessary, 'on treatment' is;

- If they are randomised to self-management;
- IF they have NOT discontinued pessary care (determined by the change of status form);
- If they have received the intervention;
- AND if they have answered Yes to question 2d (Pessary use questionnaire) "Have YOU inserted your pessary yourself in the last 6 months" at either 6,12 or 18 months"

For women in the standard clinic-based care arm of the study,

"On treatment" is:

- IF they are randomised to standard care;
- IF they have NOT discontinued pessary care (determined by the change of status form);
- AND if they have answered Yes to question 1 (Pessary use questionnaire) "Have you used a pessary for prolapse at any time in the last 6 months?" at least once at either 6, 12 and 18 months
- AND they have ticked NO to Q2d (Have you inserted your pessary in the last 6 months) at ALL time-points (6 12 and 18 months).

** Additional analysis – those who have answered yes to q2d at any time point who are in any group (standard care and self-management)

Additional analysis (to decide if standard care women are "on treatment"): If any data is missing we will assume they have answered No to Q2d

If any data is missing we will assume they have answered Yes to Q2d

3. Process evaluation

3.1 Research Questions

1) What are the:
   a) barriers and facilitators to intervention[1] acceptability for Healthcare professionals (HCP)
   b) barriers and facilitators to treatment[2] acceptability for TOPSY participating women
   c) barriers and facilitators to treatment effectiveness
   d) mediating factors impacting fidelity of intervention delivery
   e) barriers and facilitators impacting on adherence for women treated with vaginal pessary
   f) barriers and facilitators impacting on protocol adherence for the health professionals who treat women with pelvic organ prolapse
   g) identify whether barriers and facilitators differ between randomised groups
2) Investigate women's experiences of
   a) Self-management intervention
   b) Standard Care intervention
   c) Usual care out with the trial
   d) Recruitment
   e) Retention to the study and to trial arm
   f) Treatment outcomes
3) Investigate healthcare professionals' experiences of
   a) Self-management Intervention
   b) Standard care intervention
   c) Recruitment
   d) Treatment outcomes for women with prolapse
4) To identify contextual factors
   a) That help maximise recruitment
   b) That create barriers to recruitment
   c) that interact with intervention effectiveness

5. Describe fidelity to intervention delivery

6. What are factors influencing trial participation for women with pelvic organ prolapse using a pessary as treatment?

1 Intervention refers to the self-management TOPSY teaching processes

2 Treatment refers to both self-management intervention and standard care practices

3.2 Types of data

1. Audio-record self-management teaching sessions (21 audio-recordings)
    - 1-2 per centre
    - Time frame: June 2018 – February 2020
2. Audio-record 2-week follow-up phone calls (34 audio-recordings)
    - 1-2 per centre
    - Time frame: June 2018 – March 2020
3. Interviews with healthcare professionals (HCPs) (35 telephone interviews)
    - Recruiters (1 per centre) and healthcare professionals delivering the intervention (1 per centre); only 1 interview where HCP holds dual roles as recruiter and intervention deliverer
    - Time frame: August 2018 – February 2020
4. Interviews with randomised women (36 face-to-face interviews baseline (18 self-management, 18 standard care); and 23 18-month follow-up) and non-randomised women (20 telephone baseline interviews; and 18 18-month follow-up)

   Time frame: August 2018 – April 2021
5. Intervention checklist, CRF 05 (n=156)
6. 2-week follow-up call, CRF 06 (n=145)
7. Main trial Questionnaires (340 women randomised at baseline)

4. Analysis method for each data source

The process evaluation researchers are blinded to all trial data, including the analysis element of this; however, they are unblinded for all qualitative process evaluation data to which the trial team is blinded.

Each data source will be analysed individually in the first instance to reach separate conclusions and findings then synthesised across data sources. All qualitative data sources will be transcribed verbatim and entered into NVivo for data management. All of the analysis described below will be undertaken by the process evaluation subgroup of grant-holders. Analysis will not be shared with the wider grant-holding group until the main trial findings are revealed.

4.1 Recordings of teaching sessions

Recordings will be transcribed verbatim. A priori developed analytic grid based on the intervention checklist and underlying philosophy will be applied to the verbatim transcripts. The grid will contain

explicit guidance as to what codes have to be applied in what circumstances. Data will be entered into SPSS. Data will be described with the appropriate descriptive statistics: mean and standard deviation (SD) for continuous outcomes (or medians and interquartile range for skewed data), and counts and percentages for dichotomous and categorical outcomes. For example, data from the self-management teaching session and two-week follow up call will be described with a particular focus on fidelity such as the percentage of women who have been able to 1) remove and 2) replace their pessary themselves.

4.2 Recordings of 2 week follow-up phone calls

Recordings will be transcribed verbatim. A priori developed analytic grid based on the 2 week follow-up phone call CRF will be applied to the verbatim transcripts. The grid will contain explicit guidance as to what codes have to be applied in what circumstances. Data will be entered into SPSS. Data will be described with the appropriate descriptive statistics: mean and standard deviation (SD) for continuous outcomes (or medians and interquartile range for skewed data), and counts and percentages for dichotomous and categorical outcomes. For the 2 week follow-up phone call will be described with a particular focus on fidelity such as the percentage of women who have been able to 1) remove and 2) replace their pessary themselves or those who needed an additional phone call.

4.3 HCP interviews

Interview recordings will be transcribed verbatim and analysed using a Thematic Framework analysis approach – summarised below (Ritchie et al, 2013).

1. Transcript uploaded to NVivo
2. Transcript read and re-read to familiarise with content
3. Develop initial framework
4. Apply framework to all HCP interviews (adjust/amend where necessary throughout data coding)
5. Intercoder reliability will be established by having second coder independently code 10% of transcripts
6. Data extracts reviewed.
7. Data summarised and displayed using framework tables.
8. Review of preliminary “findings” involving wider research study team and PPIs
9. Data described and explained
10. Summary and presentation of findings

4.4 Interviews with Randomised women

Each participant interviewed twice (baseline & 18-month) if not lost to follow-up, withdrawn or declining the second interview.

Interview recordings will be transcribed verbatim and analysed initially using Thematic Framework analysis and then within a case study approach (detailed below).

1. Transcript uploaded to NVivo
2. Transcript read and re-read to familiarise with content
3. Develop initial framework
4. Apply framework to all interviews (adjust/amend where necessary throughout data coding)
5. Intercoder reliability will be established by having second coder independently code 10% of transcripts
6. Case summaries written
7. Theoretical propositions developed
8. Key features of data for each study condition group described
9. Comparison of study groups based on theoretical propositions.
10. Review of preliminary "findings" involving wider research study team and PPIs
11. Summary and presentation of findings

4.5 Interviews with non-randomised women

Each participant interviewed twice (baseline & 18-month) if not declining the second interview.

Interview recordings will be transcribed verbatim and analysed using Thematic Framework within a case study approach as detailed below.

1. Transcript uploaded to NVivo
2. Transcript read and re-read to familiarise with content
3. Develop initial framework
4. Apply framework to all interviews (adjust/amend where necessary throughout data coding)
5. Intercoder reliability will be established by having second coder independently code 10% of transcripts
6. Case summaries written
7. Theoretical propositions developed
8. Key features of data described
9. Comparison of groups based on theoretical propositions (women can be either self-managing or receive standard care)

10. Review of preliminary “findings” involving wider research study team and PPIs
11. Summary and presentation of findings

Case study analysis (interview data with women – randomised and non-randomised)

Each case comprises one woman and all the data gathered about that woman.

This is a three-tailed case study with the tails representing intervention and control arms of the trial respectively, as well as women who declined participation in the trial but consented to the interview study alone. Women will have been purposively sampled to reflect participant diversity (age, new/existing user, centre and potentially severity of POP and type of pessary used). The maximum total sample size will be 56 cases (20 women who only consented to the interview study [non-randomised group], 18 women in the intervention arm and 18 in the control arm). Priority will be given to complete datasets (cases which have interviews for both time points) during the analysis process. A sampling table will be populated to monitor sample diversity during the recruitment progress.

Each woman will be asked to undertake 2 interviews throughout the study duration. The first interview will be conducted at baseline and the second after 18 months. This coincides with trial data collection at baseline and at 18 months (primary outcome). For randomised women, where possible both interviews will be carried out face-to-face. Due to the COVID-19 pandemic and subsequent restrictions, all face-to-face interviews were suspended and carried out via telephone to comply with new government regulations. For non-randomised women interviews will be by phone. For women randomised to self-management, where possible baseline interviews will occur prior to their self-management teaching appointment.

The Baseline interview will explore the woman’s experience of POP and symptoms, current self-care, expectations of treatment and her experience of being recruited to the trial, and, where applicable, reasons for not consenting to the main trial but the interview study.

The 18-month interview will explore the woman’s experience of self-management/standard pessary care, experience of being taught self-management (where applicable), obstacles and complications of pessary treatment, expectations of treatment over the long term, experience of participating in the trial and adherence to trial group.

Analysis will be on four interacting levels:

1. Individual interview (steps 1-5 in interview analysis)

An a priori coding scheme will be applied that focuses on core areas of interest and which will be developed further throughout the analysis process. In particular this level of analysis focuses on women's experience of POP and symptoms; experience of self-management/standard pessary care; perceptions of treatment and causes for POP; experience of trial participation; experience of recruitment process; perceptions of treatment outcomes; adherence to trial group (where applicable); reasons for declining participation in the main trial. At this stage, the analysis is aimed at identifying barriers and facilitators to adherence to trial group, acceptability of self-management pessary care and acceptability of trial participation.

2. The case (woman) (steps 6 and 7)

Case summaries will be written with a focus on creating an understanding of women's experience in our areas of interest: the problem (POP), the treatment (self-management vs standard care), adherence to trial group (where applicable); perceptions of treatment outcome and how these factors interact. Analysis at this stage will focus on identifying issues relating to changes over time and in developing theoretical propositions to guide subsequent analysis (Yin 2013).

3. The three different arms of the interview study (step 8)

All the cases for one arm of the interview study (intervention, control, non-randomised) will be collected together and consistencies/ inconsistencies searched for. The aim of analysis at this stage is to identify the core barrier and facilitators within the trial arms, as well as, detailed explanations for them and interactions between them. An additional degree of complexity will be added by including the cases from the non-randomised women as they can be self-managing or receiving standard care.

4. Across cases and different arms of the interview study (step 9)

The intervention and control arms of the trial will be compared to one another using the theoretical propositions of the study. The aim of this part of the analysis is to identify similarities and differences between the two trial arms with regards to barriers and facilitators. Additionally, cases from the non-randomised interview only arm will be compared to the trial arms with regards to experiences of treatment and perceptions of treatment outcome. This will be conducted by comparing the arm to each individual trial arm as a whole and by separating out self-management cases for comparison to the intervention arm, and standard care cases to the control arm of the trial.

Analysis will be shared with Qualitative PMG throughout the process. At the point at which the data can be shared with the wider team it will also be discussed with PMG and TSC. Finally it will be reported to HTA.

4.6 Intervention Checklist

"Tick Box" items will be entered into SPSS and analysed by:

1. Describe the number (percentage) of use of each box ticked "yes" or "No"

2. Describe numbers for "woman was able to remove pessary" and "woman was able to re-insert pessary"

3. Crosschecking of "woman was able to remove pessary" and "woman was able to re-insert pessary" with 2 week follow-up phone call to see if women who successfully removed and re-inserted pessary during teaching sessions are more likely to have successfully removed, re-inserted and positioned pessary at home.

Free text comments from HCP will be coded using a coding framework developed using content analysis and their frequency noted. Discussions of these and descriptive statistics will be used to decide if the delivery of the self-management teaching will need to be amended after the pilot study.

4.7 2 week follow-up phone call CRF

The analysis mainly focuses on fidelity of intervention delivery and clinical acceptability. Additionally we will be monitoring how many women are transferring back to standard care after being randomised to self-management.

"Tick Box" items will be entered into SPSS and analysed by:

1. Describe number of women who successfully removed, re-inserted and positioned own pessary within 2 weeks after initial teaching session
2. Describe number of additional follow-up calls arranged
3. Describe number of additional training sessions arranged

4.8 Main Trial Questionnaires

The trial statisticians, blinded to the process evaluation data but unblinded to trial results, will undertake a statistical mediation analysis to investigate the extent to which any observed effect of self-management on women's quality of life (measured using PFIQ-7 at 18 months) is mediated by self-efficacy. Single-mediator models will individually assess the General Self-Efficacy scale and all items from pessary confidence questionnaire as potential mediating factors. The mediation analysis will use a regression-based modelling framework, with separate regression models to estimate direct effects. Indirect effects will be derived from the direct effects, with confidence intervals using Sobel's method (Sobel, 1982). This regression modelling framework will be extended to incorporate linear mixed models, specified consistently with the modelling strategy outlined in the statistical analysis plan. This will ensure the process evaluation researchers remain blinded to trial results until the appropriate time.

In addition, question 8 in the pessary use questionnaire is an open ended question and will be analysed using content analysis. A similar approach will be taken to all other free text comments provided in completed questionnaires.

5. Data synthesis across data sources and triangulation

Data synthesis will focus on the research questions where there is crossover between different data sources. The synthesis will be developed as follows (O'Cathian et al, 2010):

1. All 'findings' for each research question will be re-read.
2. A matrix was developed that outlines the data sources and the relevant research question.
3. Each source data will be summarised in the appropriate cell (cells remain blank if there is no data from that data source).
4. The agreement/ disagreement across sources will be documented in the final column.
5. A summary of key findings outlining explanation and meaning for each concept will be documented.

References

O'Cathain A, Murphy E, Nicholl J. (2010) Three techniques for integrating data in mixed methods studies. BMJ. 341:c4587. doi: 10.1136/bmj.c4587.

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Sobel, M. E. (1982). Asymptotic confidence intervals for indirect effects in structural equation models. *Sociological Methodology*, *13*, 290-312.

Yin R (2013) Case Study Research: Design and Methods. London. Sage.