C-POP Study

Exploring the feasibility and acceptability of conducting a study comparing the effectiveness of colpocleisis with sacrospinous fixation in women with pelvic organ prolapse (the C-POP study)

This protocol has regard for HRA guidance and order of content

Signature Page

Full Study Title

Exploring the feasibility and acceptability of conducting a study comparing the effectiveness of **C**olpocleisis with sacrospinous fixation in women with **P**elvic **O**rgan **P**rolapse (the C-POP study)

Short Study Title

C-POP Study

Study Protocol History

Version 1.0 25th May 2023
Version 2.0 25th July 2023
Version 3.0 20th August 2023
Version 4.0 25th August 2023

Study Protocol Amendments

Protocol Amendments				
The following amendments and/or administrative changes have been made to this protocol since the implementation of the first approved version (V1.0 25.05.2023)				
Amendment number	**Date of amendment**	**Protocol version**	**Type of amendment**	**Summary of amendment**
1	25.07.2023	2.0	Pre REC/HRA approval. Requested by sponsor.	Addition of Welsh language as an option to support Welsh speaking participants and to meet HRA/local site regulations of the Welsh Participant Identification Centre. Clarification around: gratitude wording; role of the sponsor, data protection; data analysis. Addition of end of study definition.
2	20.08.2023	3.0	Pre REC/HRA approval. Requested by sponsor.	Clarification of participant identification sites vs. recruiting sites.
3	25.08.2023	4.0	Pre REC/HRA approval. Requested by funder.	Correction to error in inclusion criteria for WP1. Clarification of end of study definition dates and study months.

Study Reference Numbers

IRAS Number:	317621
Sponsor Number:	RG 22-160
REC Number:	TBC
ISRCTN:	TBC
Funder Number:	National Institute for Health Research (NIHR151938)

Signatures

The undersigned confirm the following protocol has been agreed and accepted, and the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, relevant policies of the Sponsor, and other regulatory requirements.

The undersigned agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor.

The undersigned also agree to make the findings of the study freely available through publication or other dissemination tools without any unnecessary delay, and confirm that an honest, accurate and transparent account of the study will be given, with explanation for any discrepancies from the study as planned in this protocol.

Chief Investigator:

Signature:

Name [please print]: Dr Laura L Jones

Sponsor statement

Where the University of Birmingham takes on the sponsor role for protocol development oversight, the signing of the IRAS form by the sponsor will serve as confirmation of approval of this protocol.

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Key Study Information

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Sponsor	**Dr Birgit Whitman** Head of Research Governance and Integrity Research Strategy and Services Central Birmingham Research Park University of Birmingham 97 Vincent Road Edgbaston, Birmingham B15 2SQ Phone: 07814 650003 Email: researchgovernance@contacts.bham.ac.uk
Funder	This study is supported by funding from the National Institute for Health Research [Grant reference NIHR151938]
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	University of Birmingham Edgbaston, Birmingham B15 2TT Phone: 07786 490252 Email: e.molloy@bham.ac.uk
Committees	**Study Management Group (SMG)** Chair: Dr Laura L Jones Other members: Eleanor Molloy, Prof Carol Bugge, Prof Sarah Dean, Miss Anu Dua, Dr Pallavi Latthe, Lee Middleton, Dr Louise Jackson, Dr Lynsay Matthews, Kerrianne O'Rourke, Jacq Emkes, Melissa Kramer, Dr Melanie Dembinsky, Dr Rohini Terry, and Study Co-Ordinator (TBC) **Study Steering Group (SSG)** Chair: Professor Charlotte Clarke Other members: Dr Sarah Hillman, Dr Tina Verghese, Dr Karen Ward, Ms Angela Forrest (PPI), Mrs Anne Henderson (PPI), and Dr Lucy Frith. **Patient and Public Advisory Group** Co-Chairs: Jacq Emkes, Kerrianne O'Rourke (with support from Dr Laura L Jones) Other members: Melissa Kramer Patient members: Confidential

Study Summary

Study Title	Exploring the feasibility and acceptability of conducting a study comparing the effectiveness of colpocleisis with sacrospinous fixation in women with pelvic organ prolapse (the C-POP study).
Short title	C-POP Study
Study Design	Multi-method feasibility study aligned with the 2021 MRC/NIHR Framework for Developing and Evaluating Complex Interventions, involving four interlinked work packages (WP).
Study Participants	**Work package 1** A diverse sample of women diagnosed with apical pelvic organ prolapse (A-POP), who are able and willing to give informed consent, aged 18 years or over, and who speak English, Polish, Urdu, Punjabi, or Welsh. **Work package 2** Healthcare professionals (HCPs) involved in the care of women with A-POP (either currently or within the last 5 years) who are working in a UK complex uro-gynaecology centre, aged 18 years or over, speak English and who are able and willing to give informed consent. **Work package 3** Women aged 18 years and above, diagnosed with A-POP and eligible for both colpocleisis and sacrospinous fixation (SSF) procedures.

	Work package 4 Stakeholders including women diagnosed with A-POP, health and social care professionals, policy makers, health economists, commissioners, representatives from third sector organisations (e.g., charities and advocacy groups) in the UK, willing and able to give informed consent, over the age of 18 years and who speak English.
Planned Size of Sample [if applicable]	**Work package 1** We will seek to recruit* up to 60 women who have been diagnosed with A-POP **Work package 2** We will seek to recruit* up to 30 HCPs involving in delivering services and care to women with A-POP **Work Package 3** We do not have anticipated sample size as this work package is a cross sectional study to establish the number of women potentially eligible for a future trial. It is therefore a comprehensive account of relevant clinical activity over a 6-month period. **Work package 4** We will seek to recruit* up to 30 stakeholders for the national stakeholder event *These numbers will remain flexible to ensure that we collect sufficiently rich data to answer the research questions and achieve core analytic saturation
Follow Up Duration [if applicable]	Not applicable
Planned Study Period	Anticipated 1st April 2023 to 31st December 2024
Research Question or Aim[s]	**Overall study aim:** To explore the feasibility and acceptability of conducting a study comparing the effectiveness of colpocleisis with sacrospinous fixation in women with apical pelvic organ prolapse. This aim will be addressed via five objectives and delivered via four work packages (WP1-4). **Work Packages (WP) aims:** **WP1:** to qualitatively explore the feasibility and acceptability of the interventions and a future effectiveness study with eligible women **WP2:** to qualitatively explore the feasibility and acceptability of the interventions and a future effectiveness study with eligible HCPs **WP3:** to quantitatively explore potential numbers of women who experience this

	condition and who may be eligible for a future trial **WP4:** a national stakeholder event to gather feedback on the findings and to provide recommendations for an effectiveness trial. **Objectives:** (**1**) To explore the feasibility and acceptability of the interventions and a future effectiveness study with eligible women and HCPs (WP1,2). (**2**) To identify and explore the key uncertainties for eligible women and HCPs regarding surgical procedures for A-POP (WP1,2); (**3**) To identify and explore sensitivities and preferences for eligible women and HCPs regarding equipoise for A-POP treatment options (WP1,2); (**4**) To estimate the number of women who will be eligible to participate in a future effectiveness study (WP3); (**5**) To develop a programme theory (used to demonstrate how an intervention is expected to lead to its effects, under what conditions and for which stakeholders) and provide key design recommendations for an effectiveness and cost-effectiveness study comparing colpocleisis and SSF for women with A-POP (WP4).
Key Words	Feasibility; Acceptability; Pelvic Organ Prolapse; Apical Pelvic Organ Prolapse; Colpocleisis; Sacrospinous Fixation; Effectiveness Trial; Secondary Care; Urogynaecology; Patient Experience; Qualitative; Multi Methods

Funding and Support in Kind

Organisation	Funding or Other Support
University of Birmingham	Research sponsorship, and financial contributions to researcher salaries and support costs [e.g., IT services, telephone, printing, desk space]
University of Exeter; Glasgow Caledonian University	Financial contributions to researcher salaries and support costs [e.g., IT services, telephone, printing, desk space]
National Institute for Health Research (NIHR)	Provision of research related costs (NIHR151938)

Roles of Study Sponsor and Funder

The University of Birmingham, as the sponsor, will assume overall responsibility for conduct and management of the study. The Chief Investigator assumes responsibility for project design, data analysis and interpretation, manuscript writing, and dissemination of results. NIHR, as the funder, will contribute financial support and facilitate dissemination of the results.

Roles and Responsibilities of Study Management Committees/Groups & Individuals

STUDY MANAGEMENT GROUP

A Study Management Group (SMG) involving all co-applicants and appointed research staff (where available) will oversee the study and will meet regularly (e.g., every 1-2 months), aligned with the input needed to support successful delivery of the research. The CI (LLJ) will meet with co-applicants monthly to discuss study progress. LLJ will also meet with project research staff roughly every two weeks (as needed).

STUDY STEERING GROUP

A multidisciplinary Study Steering group (SSG) has been convened to provide independent oversight and overall supervision of the proposed research study. The SSG will provide advice to the investigators on all aspects of the study and will agree the study protocol and any protocol amendments for the duration of the project. The SSG will be chaired by Professor Charlotte Clark, Executive Dean, Faculty of Social Science and Health, Durham University.

A further six independent members including patients with experience of POP/uro-gynaecology issues; a bioethicist, and qualitative research within women's health methodologist and primary care clinician and uro-gynaecology healthcare professionals form the SSG. The SSG will meet three times during the project.

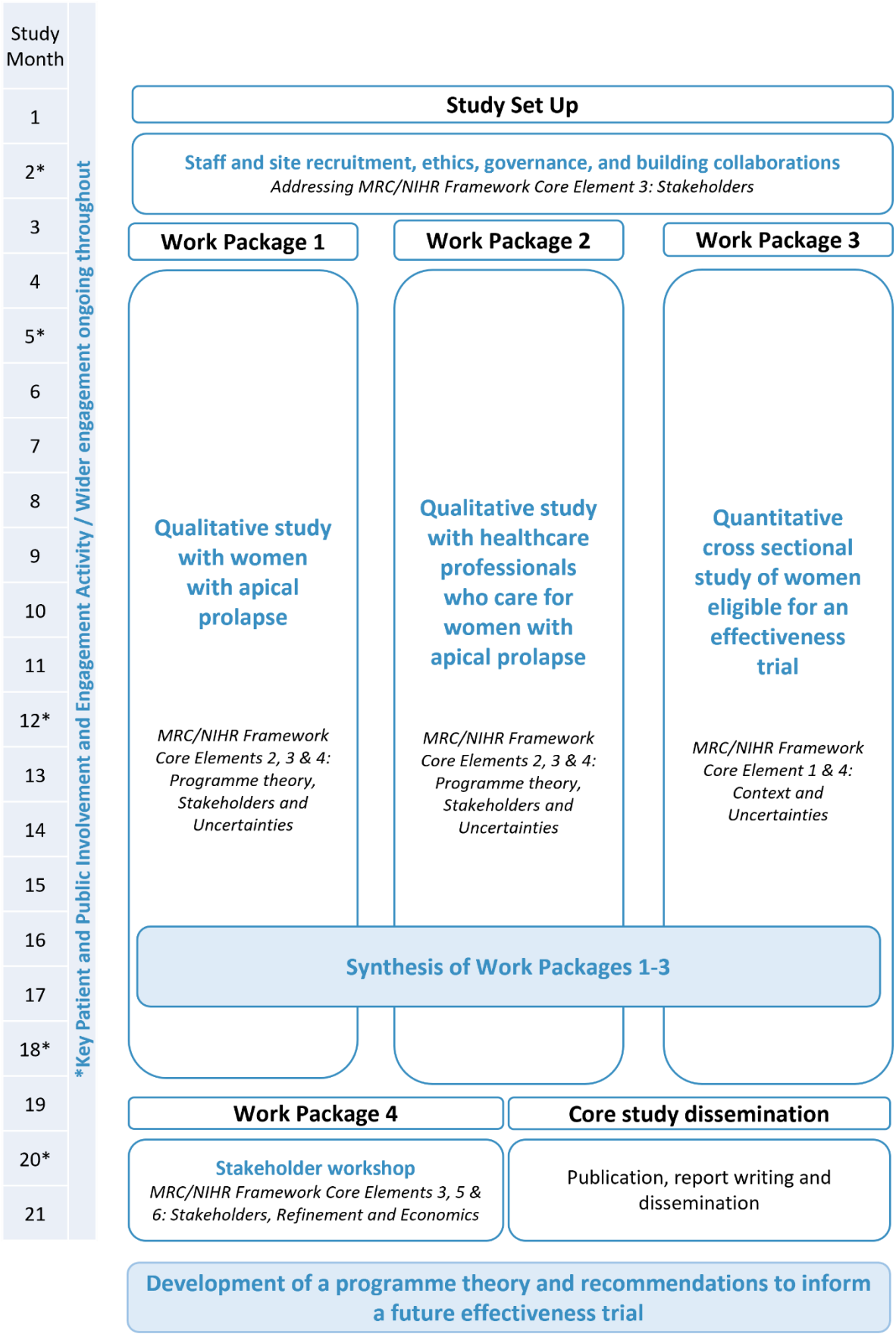
PATIENT AND PUBLIC INVOLVEMENT ADVISORY PANEL

We have established a patient advisory group (PAG) that is co-chaired by the PPI lead co-applicants (K'OR and JE) and supported by the CI (LLJ). Our PAG includes a diverse group of women with direct experience of colpocleisis and/or SSF. Please see section 6.4 for more information.

Protocol Contributors

The CI (LLJ), with the wider support of the co-investigators conceived and designed the study and drafted the original study protocol. The study protocol has undergone multiple rounds of expert peer-review as part of the funding process. All collaborators have critically reviewed version 1.0 and will actively contribute to revisions throughout the process.

Study Flow Chart



Study Gantt Chart and Milestones

Project Month	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Milestone	Description/Deliverables																					
1	Preparation and submission of application for Health Research Authority (HRA) approval via IRAS																					
2	Patient and Public Involvement and Engagement Activities																					
3	Study set up: HRA & Governance Approvals; Staff Appointments; Network Building; Identification and training of recruiters, interpreters and translators.																					
4	Submission of study protocol for publication																					
5	Work Package 1: Recruit and undertake qualitative data collection with women with apical prolapse; initial analysis (Objectives 1-3,6)																					
6	Work Package 2: Recruit and undertake qualitative data collection with clinicians involved in the care of women with apical prolaspe; initial analysis (Objectives 1-3,6)																					
7	Work Package 1 and 2: Intensive analysis																					
8	Work Package 3: Quantitative cross-sectional study exploring the potential number of eligible women for an effectiveness trial (Objective 4)																					
9	Preparation for Work Package 4																					
10	Work Package 4: National stakeholder event to finalise programme theory and recommendations for an effectivess study (Objective 5)																					
11	Finalisation of analysis, programme theory and recommendations for an effectiveness study (Objective 5)																					
12	Dissemination activities																					
13	Study Management Group (SMG) meetings																					
14	Study Steering Group (SSG) meetings																					
15	Patient and Public Involvement and Engagement (PPIE) specfic meetings																					
16	NIHR Reporting (e.g. start up, interim and final)																					

STUDY PROTOCOL

Exploring the feasibility and acceptability of conducting a study comparing the effectiveness of colpocleisis with sacrospinous fixation in women with pelvic organ prolapse (the C-POP study)

1 Background and Rationale

Pelvic organ prolapse (POP) affects 1 in 2 women(1). Apical pelvic organ prolapse (A-POP) is where the uterus, cervix, or vaginal vault bulge or hang down into the vagina. Incidence peaks at 70-79 years and negatively impacts quality of life(2). For older women with A-POP, the National Institute for Health and Care Excellence (NICE) recommends non-surgical management as first line treatment(3). If these are ineffective, surgical intervention should be considered. Surgical options for older women with A-POP are: sacrocolpopexy (performed abdominally), sacrospinous fixation ((SSF) performed via a vaginal route) and colpocleisis (performed via a vaginal route). This research focusses on SSF and colpocleisis as they are performed via a vaginal route and not sacrocolpopexy as this is performed abdominally. Although colpocleisis has lower complication and recurrence rates than SSF, it is an obliterative surgery which removes the ability to have penetrative vaginal intercourse(4). A British Society of Urogynaecology (BSUG) audit reported that SSF is associated with short term complications including: readmission within 30 days of surgery (4.4%), catheterisation for >10 days (3.1%) and return to theatre within 72 hours of surgery (0.8%)(5). The number of SSF and colpocleisis procedures has increased year on year, with almost four times as many SSFs compared to colpocleisis in 2021 (860 vs. 186 respectively)(6). To date there is no evidence to say why colpocleisis is undertaken less commonly but possible explanations include: lack of equipoise of clinicians; that colpocleisis is ‘end-of-the-road’ surgery; uneasiness with obliterative surgery; or unfamiliarity with the surgical technique. Given the uncertainties, this is an opportune moment to compare the effectiveness and cost-effectiveness of colpocleisis compared to SSF via a randomised controlled trial (RCT). However, views of key stakeholders are needed to explore if a future effectiveness trial is feasible and acceptable.

1.1 Review of existing evidence

The NIHR HTA has extensively reviewed the evidence base for the commissioning brief. In addition to this, a scoping search of the relevant literature was undertaken via databases including Medline, Embase and CINAHL, using key search terms such as “apical prolapse”, “pelvic organ prolapse”, “colpocleisis”, “sacrospinous fixation”. The evidence identified was used to inform the development of the C-POP study, including the study design and to identify key uncertainties to be addressed as part of the study.

Within the evidence, six key uncertainties were identified.

1.1.1 **Patient characteristics**: A narrative review (n=49 studies) by Gryzbowska *et al.*(7) showed the mean patient age for colpocleisis ranged from 69.0 ± 8.0 to 84 ± 3.1 years. The oldest patients undergoing surgery were 95.9 and 101 years. In the studies by Krissi *et al.*(8) and Mueller *et al.*(9), women aged >80 years constituted 49% and 43% of the total patient population respectively. Colpocleisis may also be performed in younger women with comorbidities to manage advanced POP. In a large database of 4,776 participants, colpocleisis was found to have been performed in 47 (0.9%) patients aged 20–39 years(9). Several studies report the median age of SSF as 63 years. Although the data shows the mean patient age for colpocleisis is >69 years, several studies report the median age for SSF as lower, at 63-65 years of age(10, 11). We will therefore include women with A-POP, irrespective of age, who are clinically eligible for surgical intervention in this study. This will ensure meaningful data are collected about the feasibility of a future trial for different age ranges. Our PPIE highlighted that it was important to include women eligible for surgery regardless of age, although women <69 years of age may be small in number.

1.1.2 **Decision making for women and HCPs**: Flynn *et al*.(12) suggested that the choice of POP surgical procedure should consider the individual surgeon's experience, the patient's age, co-morbidity, previous surgery and the level of physical and sexual activity. However, due to the obliterative nature of colpocleisis understanding the decision-making processes of women and HCPs is important. As far as the applicants are aware, there are no studies exploring clinician equipoise around SSF and colpocleisis. This is a key uncertainty for C-POP as clinician equipoise is typically required for a future trial to be feasible. Further to this, few studies explore women's decision-making around colpocleisis. It is important to explore this within C-POP. A qualitative study (n=10 older Caucasian women) reported that women primarily made the decision to have surgery autonomously(13). None regretted having colpocleisis for reasons of sexual function loss (coital regret was low). They felt positive about the ability to control their body through their own decision. Women felt adequately counselled regarding other options and the surgical procedure. Many patients wished they had pursued surgery earlier because they were very satisfied with the results. Although women in this study were happy with their decision, this is only one small study in a sample of older Caucasian women. We found no studies reporting the decision-making processes of women undergoing SSF. Numerous uncertainties therefore remain around the decision-making processes for A-POP surgery including: (i) whether previous pelvic floor surgery influenced their decision; (ii) the impact of postoperative complications on their level of perceived regret; (iii) the process of decision making in a non-Caucasian population; and (iv) the experience of decision-

making and perceived regret (e.g., coital regret) in women who decline to participate in such follow-up studies. We will explore each of these uncertainties within C-POP.

1.1.3 **Sexual function**: Sexual dysfunction and dyspareunia (painful sex) are common symptoms of POP. A study of 110 women in Germany, with a median age of 63 years (range 39-89 years), reported 55% (n=61) were sexually active before SSF surgery(11). Following SSF, most of these women reported improved sexual function. This is supported by Yalcin *et al*.(14) who, in a study of 26 sexually active women, observed a significant improvement at 6-months post-SFF in multiple aspects of sexual functioning (i.e., the behavioural emotional factor, physical factor, and partner-related factor as measured by the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire *PISQ-12*). Colpocleisis, however, is an obliterative surgery meaning that women are no longer able to engage in penetrative vaginal sex although then can still engage in other sexual activity. Consideration of future penetrative sexual activity is a central feature of decision-making (see section 1.1.2). Deval found that 52% of 30 women remained sexually active after colpocleisis by means of clitoral stimulation(15). A recent study by Wang *et al*.(16) explored the reasons for sexual inactivity in a sample of 247 women (mean age 73.8 ± 5.58 years). The mean duration of sexual inactivity was 12.6 ± 8.69 years, with most women giving the reason as being widowed (52%), followed by the physical health of their partners (37.2%), their own health (5.3%) or a combination of both (5.3%). When 78.9% of this sample were followed-up post-operatively 98.5% were very satisfied and perceived an improvement in their symptoms. Only 2 of 195 women regretted colpocleisis 2 years later. General decision regret (not related to sexual function) ranged from 0% to 13.8% with main reasons being POP recurrence, urinary incontinence, or postoperative complications(7). Regret related to sexual function was low, with most studies reporting no regret regarding loss of penetrative coital ability. In those that do report coital regret, rates ranged from 1.2% to 12.9%. In a study (n=79) by Fitzgerald et al(17), 3%, 87%, and 10% of the women reported “worse,” “the same,” or “better” sexual function respectively, after 1 year of follow-up. We will explore the influence of coital status and the reasons for this on decision making around surgical intervention with women as part of C-POP. Our PPIE discussions highlighted that many women may not be having penetrative sexual intercourse prior to surgical intervention due to their POP symptoms and so surgery might improve sexual activity even without penetrative vaginal intercourse. It is known that culture and religion play a role in seeking help for health issues(18), with particular emphasis on sexual health(19). Seeking help for symptoms of sexual dysfunction or speaking about sexual activity may be viewed negatively. This is an important issue to navigate when caring for women from a range of cultural and ethnic backgrounds. There is little in the

literature to suggest best practice for such encounters. Speaking to women about sexual activity is therefore a key uncertainty to be explored within C-POP, both by PPIE and with research participants. Our approach will be informed by the '*Religion or Belief: A practical guide for the NHS'* resource(20).

1.1.4 **Recruitment of older women**: It can be challenging to recruit older participants to clinical research, including trials. Goode *et al.*(21) explored recruitment and retention of older women with POP in two surgical trials. Using focus groups and questionnaires with HCPs, findings indicated it was more difficult to recruit older research participants (32%), obtain informed consent (56%), and retain participants to study completion (50%). Challenges to recruitment included caregiver involvement in the decision to participate and participant comorbidities. Our PPIE identified that carers play an important role in decision making and can be impacted because of surgery such as in relation to sexual activity. Perceived barriers to retention were transportation, caregiver availability, and participant fatigue. Data quality was challenged by sensory and cognitive impairment, resulting in a change from telephone interviews to in-person visits. Older participants (>75yrs) did not have higher dropout than younger participants (<75yrs). There were no differences in number of missed in-person visits or telephone interviews between age groups. Participants over the age of 75 years have been identified as an underserved group by NIHR's INCLUDE project(22). We will therefore embed strategies to maximise the likelihood of older participants being recruited to our study, informed by the evidence base and by our PPIE. For example, by addressing the challenges reported by Goode(21), by using guidelines such as the Health Inequalities Assessment Toolkit(23), and by meaningful engagement with PPIE stakeholders before and throughout the study (see PPIE section 6.4). Overall, these are important considerations that will need to be addressed as part of our recommendations as to whether a future trial is likely to be feasible and accessible.

1.1.5 **Effectiveness of and satisfaction with colpocleisis and SSF**: Grzybowska's review (n=49 studies) demonstrated positive findings in relation to surgical 'success' and patient 'regret'(7). Anatomical success, defined as: (i) POP-Q stage ≤ 1, was achieved in 62.5 to 100%; and (ii) no prolapse beyond the hymen, was achieved in 87.5 to 100% of all patients. Subjective success judged by women ranged from 88% to 100%. Lu *et al.*(24) explored long-term clinical outcomes, recurrence, satisfaction and regret after total colpocleisis (and hysterectomy). They found that, in a sample of 242 older women, only one reported recurrence of POP. Similar results were found in a long-term follow-up by Wang *et al.*(25) who found no anatomical recurrence in their sample of 208 women, and a re-operation rate of 1.44%. Although the evidence base for SSF also demonstrates

effectiveness a long-term follow-up study of 59 women reported a POP recurrence rate of 22% at 5-years post-SSF(26). Subjective satisfaction of colpocleisis was high and degree of regret was minimal. This is further supported by Ertas *et al*.(27) in a retrospective study of 53 women who underwent colpocleisis, where they found positive anatomic outcomes, a significant decrease in POP-Q scores and a lack of regret. They concluded colpocleisis should be considered as a first-choice procedure for older and sexually inactive women with advanced POP. However, it is important to consider that this was a study of sexually inactive women and that women can be sexually active (like members of our PAG) and still undergo colpocleisis. The surgery results in a lack of ability to have penetrative vaginal sex but does not prevent other types of sexual activity.

1.1.6 **Risks and side effects**: The rates of complications and Intensive Care Unit (ICU) admissions following colpocleisis are low, with mean rates of 6.8% and 2.8% respectively(9). Urinary tract infection (UTI) is the most common postoperative complication (28). This is supported by Grzybowska's review, also showing that UTI is the most common postoperative complication (4.3 to 9% confirmed with urine culture, 34.7% based on symptom definition)(7). Bowel injuries (0 to 2.7%) and urinary tract injuries (0 to 9.1%) are rare complications, absent in most studies, and typically the consequence of concomitant procedures(7). Rectal injuries are usually sutured during surgery(29). Mortality rates from colpocleisis are low. Based on data from 145 US medical centres, the 30-day mortality rate was 0.15%(9). In a multi-centre study among 152 patients, the rate was 0.65%, with one death five months after surgery as a result of sepsis and congestive heart failure(30). Risks and side effects of SSF are also documented. In the BSUG audit of 10,557 NHS patients (2008-2017)(5), peri-operative SSF complications included blood loss of >500 ml (0.9%), bladder injury (0.3%) and bowel injury (0.2%). Post-operatively, 4.4% were readmitted within 30 days of surgery, 3.1% required catheterisation for >10 days, and 0.8% returned to theatre within 72 hours of surgery (0.8%)(5). Like colpocleisis, mortality rates for SSF were low, with one death recorded in the audit of 10,557 women (0.01%).

In summary, SSF and colpocleisis are increasingly offered as management for A-POP. Although SSF is performed more frequently than colpocleisis, data demonstrates that colpocleisis is becoming more common in the UK NHS. It is associated with low rates of adverse events and low decisional regret. The population of women who are eligible for this procedure tend to be older women. There are known challenges of recruiting this population into research studies. Many uncertainties remain in the comparison of SSF and colpocleisis. C-POP aims to explore these uncertainties.

2 Why is this research needed now?

A combination of the prevalence of A-POP, older age of the women (an NIHR identified underserved group within research), approximate £45 million annual cost to the NHS, and the potentially life changing consequences of the surgery contribute to the importance of establishing the best evidence for treatment. There is currently no direct efficacy, effectiveness, or safety comparison between colpocleisis and SSF. This is a key research priority for the RCOG and NICE(3, 31). The most recent NICE guideline stated that exploring the effectiveness of SSF versus colpocleisis is a research priority(32).

This research is important for three key reasons. Firstly, POP, including A-POP, is a major cause of morbidity in women(33). QoL and symptoms can be improved following surgery, but which surgery is most effective is currently unknown. Secondly, POP places a significant economic burden on women and the NHS(34). For example, up to 30% of POP repairs require further surgery(35). If colpocleisis is found to have a high success rate and very low complication rate, it may be more acceptable, as well as more clinically and cost-effective, compared to a reconstructive procedure such as SSF. Finally, there is no clear evidence of women's and HCP views about SSF and colpocleisis that would ensure that a trial, and any future service implementation, is grounded in what women and HCPs want and what is practical for the NHS.

3 Theoretical Framework

Aligned with the 2021 MRC/NIHR framework for Developing and Evaluating Complex Interventions(36, 37), this study will undertake a ***feasibility*** exploration, using a ***theory-based*** perspective(36). The six core elements of the framework are embedded throughout the protocol. How they are addressed is outlined in Table 1. The core elements are highlighted in bold square brackets throughout this protocol (e.g., **[Core element 1: Context]**).

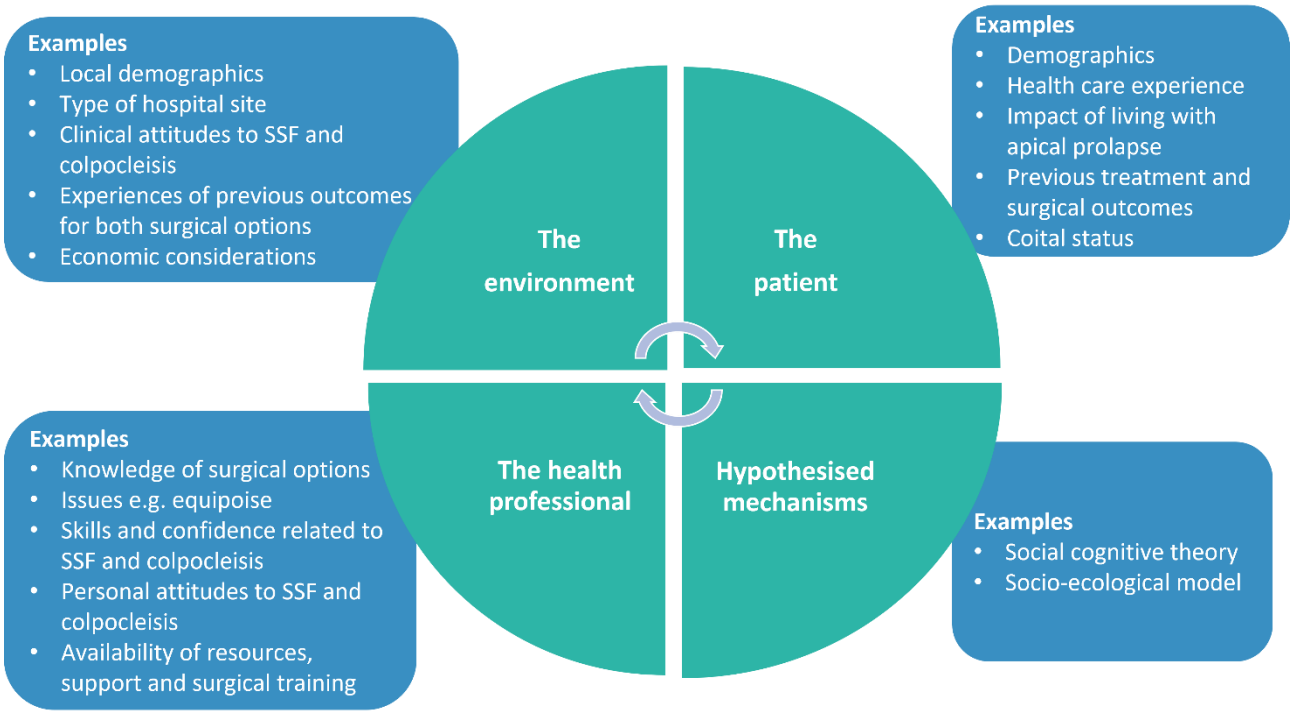
Table 1. ***How does this study align with the 2021 MRC/NIHR Framework****(36)****?***

Core element	Inclusion
1. Considering context	Multiple aspects of context have been considered to inform an initial programme theory. Contextual factors relate to patients, HCPs, setting, cultural, economic, and political factors.
2. Developing and refining programme theory	A draft programme theory (Figure 1) has been developed to inform the C-POP study. It addresses a theory-based perspective incorporating context at multiple levels (as above), alongside potentially relevant theories and frameworks related to feasibility and decision making.
3. Engaging stakeholders	Insight from a range of stakeholders has informed the development of the C-POP study, including input from a multidisciplinary research team and five patients. The study is set up to keep all stakeholders, in particular women with A-POP, central to the study developments.
4. Identifying uncertainties	We will explore uncertainties about the intervention and the trial processes, for women and HCPs, including issues related to decision-making; equipoise; feasibility and acceptability.

5. Refinement	Although the proposed study does not involve 'refinement of an intervention' our proposed approach does involve refinement of trial processes in further stages of research (e.g., methods of engaging with older participants, accessible formats of trial resources, how to explain the two surgical procedures to ensure equipoise for the RCT etc.)
6. Economic considerations	We have a co-applicant health economist (LJa) to inform the economic components of the study's programme theory and to ensure appropriate health economic data are collected to inform progression to further stages of research.

We have drafted an initial programme theory (see Figure 1) for the feasibility and acceptability of a future effectiveness trial. This is based on the evidence provided as part of the commissioned call and our scoping review of the evidence base. The MRC/NIHR Framework(36) states that "*a programme theory is used to demonstrate how an intervention (e.g., a trial) is expected to lead to its effects and under what conditions. It articulates the key components of the intervention and how they interact, the mechanisms of the intervention, the features of the context that are expected to influence those mechanisms, and how those mechanisms might influence the context(38)*." Further to this "*a programme theory can be used to promote a shared understanding of the intervention (e.g., a trial) among diverse stakeholders and to identify key uncertainties(39)*." As we gather data, the draft programme theory will be revised and refined to produce a final programme theory. This can then be used to inform a future effectiveness trial.

Figure 1. Draft programme theory for feasibility and acceptability of the C-POP study



4 Research Aims, Objectives and Outcomes

4.1 Overall Study Aim

To explore the feasibility and acceptability of conducting a study comparing the effectiveness of colpocleisis with SSF in women with apical pelvic organ prolapse. This overarching aim will be addressed via five objectives linked to the 2021 MRC/NIHR framework(36) (see Table 1 and Figure 1) and delivered via four work packages (WP1-4).

4.2 Objectives

(1) To explore the feasibility and acceptability of the interventions and a future effectiveness study with eligible women and HCPs (WP1,2) **[Core elements 1, 3 & 4: Context, Stakeholders & Uncertainties]**

(2) To identify and explore the key uncertainties for eligible women and HCPs regarding surgical procedures for A-POP (WP1,2) **[Core elements 3 & 4: Stakeholders & Uncertainties]**

(3) To identify and explore sensitivities and preferences for eligible women and HCPs regarding equipoise for A-POP treatment options (WP1,2) **[Core elements 2, 3 & 4: Programme theory, Stakeholders & Uncertainties]**

(4) To estimate the number of women who will be eligible to participate in a future effectiveness study (WP3) **[Core element 4: Uncertainties]**

(5) To develop a programme theory and provide key design recommendations for a future effectiveness and cost-effectiveness study comparing colpocleisis and SSF for women with A-POP (WP4) **[Core elements 3, 5 & 6: Stakeholders, Refinement & Economics]**

4.3 Outcomes

The final programme theory will provide clear guidance, informed by novel insight from women, HCPs, and diverse stakeholders, on the feasibility of and key considerations for a future effectiveness trial.

Data will include specific insight on:

(i) the issue of coital status for women of various ages and different cultural backgrounds

(ii) sensitivities, uncertainties and preferences of women and HCPs regarding treatment options for A-POP

(iii) the number of eligible women for a future trial and

(iv) potential mechanisms for feasibility and acceptability of a future trial

If findings from C-POP demonstrate a future trial is feasible and acceptable, the resulting programme theory and recommendations will form the basis for a robust trial protocol that is well-developed and

deliverable. C-POP data and a subsequent trial would inform future clinical practice and guidelines.

5 Study Design, Methods of Data Collection and Analysis

5.1 Study Design

This study has been designed as a multi method feasibility study aligned with the 2021 MRC/NIHR Framework for Developing and Evaluating Complex Interventions(36, 37). The C-POP study will be delivered via four work packages which are outlined below (sections 5.2-5.5)

5.2 Work Package 1: Qualitative study of women with A-POP (objectives 1-3, 6)

5.2.1 DESIGN

Descriptive qualitative study

5.2.2 TARGET POPULATION

Adult women, and individuals assigned female at birth (AFAB), who have been diagnosed with A-POP and who are eligible for or who have had colpocleisis and/or SSF. Please note that all women with A-POP who are eligible for colpocleisis would also be eligible for SSF.

5.2.3 SAMPLE SIZE

Anticipated 50-60 participants recruited across the anticipated eight sites (recruitment numbers are likely to vary by site dependant on the number of patients they care for) and via the supplementary recruitment pathways described in section 5.2.4. ***Justification for sample size:*** Numbers will remain flexible to ensure that the overall sample and associated data have sufficient information power to develop new knowledge in relation to the research questions(40). This approach will also help identify if we can engage and recruit from multiple sites, in different UK locations, for any future RCT. Although 50-60 is a relatively large sample in descriptive qualitative studies, this is key to help facilitate diversity in the sample of women approached and participating. This will ensure that the findings are likely to be transferable to the wider UK A-POP population.

5.2.4 SAMPLING AND RECRUITMENT

Potential participants will be recruited via a range of pathways to facilitate diversity and heterogeneity, and to ensure that we can achieve our recruitment targets. We have support from the West Midlands Clinical Research Network (CRN) who will work alongside other CRNs to support our recruitment. Women (and

those AFAB) will be identified via (1) face to face discussions and adverts in clinics within the anticipated eight sites across the UK (see below), (2) a direct letter from their clinician if they have had colpocleisis or SSF within the last six months, (3) social media advertising, (4) advocates in Community and Voluntary Organisations (e.g., Bladder Health UK, liveUTIfree, Pelvic Obstetric and Gynaecological Physiotherapists (POGP), Bristol Health Partners – Bladder and Bowel Confidence BABCON), and (5) snowballing.

Potential participants will be identified from an anticipated eight diverse Participant Identification Centres (PICs) across the UK complex uro-gynaecology centres performing A-POP surgery and who reported data to the BSUG audit database 2019-2022. The anticipated eight sites are likely to include (but may change) Birmingham, Bristol, Cornwall, Coventry, Glasgow, Plymouth, Sheffield, Shrewsbury, Swansea. Further to this, the chairs of the BSUG research network and the RCOG have also agreed to support the study and help us to promote recruitment and to identify additional sites should this be needed to ensure successful delivery of the study. Sites have been purposively sampled to reflect and ensure diversity in the potential participant population informed by data from the BSUG database. These include sites with high disease burden, underserved populations, those who have historically been inactive in this research area, and where co-applicants are based **[Core element 1: Context]**.

Participants will be categorised into three subgroups: (1) women who have previously undergone colpocleisis; (2) women eligible for colpocleisis who have not had previous surgeries; and (3) women eligible for colpocleisis who have had previous failed A-POP surgery(ies). A maximum variation sample will include ethnicity, age, comorbidities, previous POP treatment history, type of service and location **[Core element 1: Context]**.

Women who see an advert for the study will be asked to contact the research team directly (e.g., via phone, email, social media) to discuss participation and be screened for eligibility. Women approached by a member of their usual care team will be asked to give permission for the C-POP team to contact them by completing a consent to contact form which will be either completed via ReDCAP or completed on paper and scanned/photographed and sent via secure e-mail, and/or will be given the research teams contact details so that the women can approach the team directly. Although social media may not be a key route of recruitment for older women (as informed by our PPIE and the evidence base) it may reach some of the women and/or other people in the woman's social circle who can inform them of the study and does offer the potential of recruitment beyond the anticipated eight sites.

For participants whose first language is not English, participant information leaflets, background questionnaires, and consent forms will be available in alternative languages (including Polish, Urdu Punjabi, and Welsh) to support the informed consent process and data collection. Polish, Urdu and Punjabi were identified as the three most spoken languages in the UK after English and are likely to be inclusive of many

women with A-POP(41).

5.2.5 ELIGIBILITY

(i) Inclusion criteria: Female (or AFAB), age 18 years and above, diagnosed with A-POP, eligible for both colpocleisis and SSF procedures (or have already had one or both surgeries previously), ability to provide informed consent, able to communicate in either English, Polish, Urdu, Punjabi or Welsh. *(ii) Exclusion criteria:* None. ***Rationale for eligibility criteria:*** The aim of this study is to explore the ***feasibility*** of a trial comparing colpocleisis with SSF. An upper or lower age limit could omit meaningful insight from women of different ages. Colpocleisis is typically performed in women >69 years, therefore we intend to actively attempt to recruit and interview women <69 years to gather their insight. We will also specifically ask recruiting sites to identify eligible younger women (e.g., <60 years).

5.2.6 CONSENT

Following initial contact with the participants, a member of the research team (based in one of the three C-POP recruiting sites: University of Birmingham, Glasgow Caledonian University, or the University of Exeter) will liaise with participants via telephone, SMS, social media and/or email, to discuss the research, answer any questions about taking part, confirm eligibility, and arrange a suitable opportunity for an interview.

Eligible interview participants will be invited to take time to consider participation carefully. It will be made clear that involvement in the study is voluntary and that they are free to withdraw up to two weeks after the data collection event without giving a reason. They will also be reassured that their participation will be kept in the strictest confidence (apart from disclosure of certain activities, for example, where individuals may be at risk of harm that requires further action).

For participants whose first language is not English, participant information leaflets, background questionnaires, and consent forms will be available in alternative languages to support the informed consent process. For those who decide to take part, participation instructions and appointment reminders will be sent via email, SMS, social media or via phone ahead of each interview. For those who wish to participate via a phone interview a participant information leaflet, background questionnaire, and consent form (in an appropriate language) will be sent via post/email ahead of the scheduled interview with instructions on how to complete the forms and return them to the research team.

Written informed consent will be sought wherever possible. However, for example, in cases where the study related paperwork has not been received, not fully completed, or there are issues around literacy or technological naivety, then we will seek alternative forms of informed consent including electronic (e.g., JISC Online Surveys link, or electronic completion and scanning/photo of the consent to participate form) or

verbal (e.g., where the consent form will be read out in full, and audio recorded at the start of the interview to be recorded in a separate audio file to the main discussion).

Informed consent (including written, electronic and/or verbal) will gain permission for agreement to participate, demographic data collection, audio recorded dialogue of discussion, and pseudo-anonymised data sharing. At the beginning of each audio recording, participants will be asked to verbally (re-) confirm consent. Where formal verbal informed consent is being sought at the start of an interview, then the audio recorder will be switched on and the consent form will be read out, and the participant asked to consent to each statement. Should the participant not consent to any of the statements then the interview will be terminated at that point having explained to that participant that data collection cannot continue, as they have not consented to participate.

5.2.7 DATA COLLECTION

As informed by our PPIE, semi-structured interviews will be conducted to facilitate an in-depth exploration of women's views and experiences(42). Interviews will be conducted in a participant-focused manner allowing experiences important to participants to develop naturally(43). Discussion guides will be developed iteratively to ensure that a range of views are captured and initial analysis and interpretations tested(44). Discussions will primarily focus on (i) acceptability of the treatment options; (ii) acceptability of the proposed trial processes, including equipoise, randomisation, outcome measures, cost/resource use measures etc.; and (iii) feasibility of trial delivery **[Core element 4 & 6: Uncertainties, Economics]**. Additional issues to be explored include decision making; women's thoughts on surgical intervention versus non-surgical procedures; their preferences and sensitivities regarding treatment options; issues related to sexual health and wellbeing; and barriers and facilitators to participation in a future trial.

Our PPIE highlighted the importance of giving potential participants choice. Participants will therefore be given the choice to see the interview question list in advance of participation, allowing participants to familiarise themselves with the main topics for discussion and raise any queries with the team in advance of the interview. Participants will also be given the choice as to where and how an interview takes place (e.g., via phone, video call, or face to face at home, in clinic or other appropriate private space)(45). Our PPIE has shown that there is a need for a face-to-face option and that this is likely to be the main data collection method. We anticipate that whilst most interviews will be face to face, we will ultimately use a blended approach of face-to-face, phone and virtual data collection, via approved University accounts, given the need for COVID resilience, minimising travel implications and the facilitation of interviews in a relatively short time frame. We will also ensure that women are supported to participate, for example, by sending out guidance and offering a "trial run" with a researcher to ensure that they know what to expect. Further to this, if participants need support (e.g., from a carer) to participate in an interview/attend an

interview appointment we will support this by covering travel expenses and their time (e.g., via a £25 High Street shopping voucher, which will be made available as physical or online depending on participant preferences). The carer may be present for the interview with the woman's permission, although they will not be formally consented and will not be invited to contribute to the discussion.

Interviews will be conducted by a trained qualitative researcher who will be independent of the participant's clinical care team. Researchers will use field notes to document descriptive and interpretive data informed by their interview observations(46). Professional interpreters, who will receive specific training around POP by the research team (with support from PPIE) will be employed to provide real-time oral translation services during the interviews where there is a language barrier between the researcher and the participant. Interpretation will focus on semantic and conceptual equivalence across the languages (English, Polish, Urdu, Punjabi, and Welsh) rather than direct word for word interpretation and a translation lexicon will be developed(47, 48). A debrief between the researcher and the interpreter will be held after each interview to identify any interpretation issues, as appropriate.

Data collection will be guided by Dempsey *et al.'s* framework of essential elements for conducting qualitative research given the potentially sensitive issues, including those around sexual function, that may emerge in discussions(49). Participants will also be asked to complete a demographic questionnaire to facilitate maximum variation sampling and a description of the characteristics of the overall cohort. Maximum variation within the sample will be routinely reviewed (e.g., at the fortnightly project team meetings). Participants will be offered a £25 voucher to thank them for their time and expenses covered where a woman (including a further £25 voucher and expenses for her carer as appropriate) has travelled to an interview appointment.

5.2.8 DATA ANALYSIS

Interviews will be audio recorded (please note if video conferencing software is used to support the interview, only the audio will be recorded and not the video) and transcribed clean verbatim by a specialist GDPR compliant transcription company, which has a confidentiality agreement in place with University of Birmingham. Telephone or face to face interviews will be recorded using handheld digital encrypted voice recorders. Audio files which are created by teams at University of Exeter or Glasgow Caledonian University will be downloaded to the Dictation Software Management System on secure, encrypted University owned laptops. Each audio file will then be uploaded to a secure OneDrive SharePoint folder for transfer to University of Birmingham and the transcription company. These folders will only be accessed by people with relevant authority (i.e., LJ and EM). Once the recording has been confirmed as being uploaded and transferred to the transcription company it will be deleted from the recording device.

Once quality checked and anonymised, transcripts will be imported into NVivo software to facilitate data

management. Where resources allow, up to eight transcripts (two Polish, Urdu, Punjabi, and Welsh) will have both the English and second language translated and transcribed. For all other multi-language interviews, only the English parts of the discussion will be transcribed. Early translation (i.e., prior to the start of data analysis) is recommended as it facilitates a more interactive process of data analysis between researchers and interpreters/translators and helps to inform future data collection(50).

Data (including transcripts, researcher field notes and reflexive accounts) will likely be analysed using a reflexive thematic analysis approach (RTA)(51), aligned with the elements of the 2021 MRC/NIHR framework(36). The six phases of RTA will be followed: (1) data familiarisation, (2) initial code generation, (3) generating (initial) themes, (4) theme review, (5) theme defining and naming, (6) report production. A hybrid approach, using both inductive and deductive coding will be used to explore depth, richness, and quality of the data. Deductive codes will be guided by the C-POP study draft programme theory (see Table 1 and Figure 1) and the six core elements of the MRC/NIHR framework. Multiple researchers will be involved in the analysis process to facilitate analyst triangulation(52). Initial analysis will be discussed as part of our PPIE and with the wider research team to ensure multiple worldviews and perspectives can contribute to and support interpretation. Demographic data will be reported descriptively.

5.3 Work package 2: Qualitative study of HCPs involved in management of A-POP (objectives 1-3,6)

5.3.1 DESIGN

Descriptive qualitative study.

5.3.2 TARGET POPULATION

HCPs across the UK involved in the care of women with A-POP who are eligible for surgery/have received surgery previously, those who would be involved in a potential future trial, including but not limited to, doctors of various specialities and grades, nurses in various roles such as practice nurses, advanced gynaecology and urogynaecology nurse specialists.

5.3.3 SAMPLE SIZE

Anticipated 20-30 participants. ***Justification for sample size:*** Numbers will remain flexible to ensure that the overall sample and associated data have sufficient information power to develop new knowledge in relation to the research questions(40). This approach will also help identify if we can engage and recruit from multiple sites, in different UK locations, for any future RCT.

5.3.4 SAMPLING AND RECRUITMENT

HCPs will be recruited via a range of pathways to facilitate diversity and heterogeneity in characteristics and skillset, and to ensure that we can achieve our recruitment targets. These include: (1) HCPs identified from across the UK complex uro-gynaecology centres performing SSF and/or colpocleisis surgery including the anticipated eight sites involved in WPs 1 and 3; (2) the C-POP study teams' personal and professional networks; (3) snowballing; (4) advertising on social media, and (5) appropriate mailing lists such as BSUG and RCOG. Maximum variation sampling will include type of centre, numbers of surgeries performed, level of experience, surgical vs. non-surgical HCPs, and location/geographical spread **[Core element 1: Context]**. Maximum variation within the sample will be routinely reviewed (e.g., at the fortnightly project team meetings). Participants will be offered a £25 voucher to thank them for their time.

5.3.5 Eligibility

(i) Inclusion criteria: UK based secondary care HCPs involved in the care of women with A-POP (either currently or within the last 5 years); working in a UK complex uro-gynaecology centre; able to give informed consent and speak English. *(ii) Exclusion criteria:* HCPs based in primary care. ***Rationale for eligibility criteria:*** This sample ensures data are gathered from HCPs who would likely be involved in a future effectiveness trial.

5.3.6 CONSENT

As per work package 1.

5.3.7 DATA COLLECTION

Phone, video conference or face to face semi-structured interviews will be conducted (as for WP1) to explore: (i) acceptability of the treatment options for HCPs; (ii) acceptability of the proposed trial processes for HCPs, including their willingness to accept randomisation of patients in their care; (iii) feasibility of trial delivery and collection of data on the resource use and costs associated with treatment options; and (iv) issues related to equipoise when discussing options with patients **[Core element 4: Uncertainties; Core element 6: Economics]**. Additional issues to be explored include HCP perceptions of which patients are eligible for colpocleisis; barriers and facilitators to being involved in a trial; potential primary and secondary outcomes and meaningful progression criteria. Participants will be given the choice to see the interview question list in advance of participation, allowing participants to familiarise themselves with the main topics for discussion and raise any queries with the team in advance of the interview.

5.3.8 DATA ANALYSIS:

Data will be analysed as for WP1 (except for translation as all interviews will be in English).

5.4 Work package 3: Quantitative cross-sectional study exploring the potential number of eligible women for an effectiveness trial (objective 4)

5.4.1 DESIGN:

Cross sectional study.

5.4.2 TARGET POPULATION:

Women and individuals assigned female at birth (AFAB), who have been diagnosed with A-POP and who are eligible for colpocleisis and SSF (see section 5.4.5).

5.4.3 SAMPLE SIZE:

Comprehensive account of relevant clinical activity over a 6-month period.

5.4.4 SAMPLING AND RECRUITMENT:

Potential participants will be identified from an anticipated eight diverse participant identification sites from UK complex uro-gynaecology centres performing A-POP surgery and who reported data to BSUG 2019-2022 as per WP1.

5.4.5 ELIGIBILITY

All females (or AFAB) age 18 years and above, diagnosed with A-POP and eligible for both colpocleisis and SSF procedures (i.e., no longer intend to have penetrative vaginal intercourse and who are willing to have either surgical procedure) will be included. ***Rationale for eligibility criteria:*** This sample ensures we gather data to inform feasibility of recruiting to a future effectiveness trial. We do not intend to screen for potential exclusion criteria at this stage.

5.4.6 DATA COLLECTION

Site researchers (e.g., local research nurses) will collect anonymised data on women meeting the eligibility criteria via scrutiny of referral letters and clinic notes. Sites will be asked to report these data a minimum of once a month during the six-month data collection window, but can do this at a frequency (e.g., weekly, every two weeks) that suits their local clinical set up and resources. Data will be recorded in an anonymous screening log/proforma and sent securely to the C-POP research team at University of Birmingham. As part of the site initiation visits and study set up, the C-POP research team will work with the site to establish the best ways to record and send these data. Demographic information available in notes (e.g., age, ethnicity, postcode (as a marker of deprivation) and first language) will also be collected to enable characterisation of the potential trial population.

5.4.7 DATA ANALYSIS

GDPR-compliant data will be sent securely to the central C-POP team for collation and analysis using descriptive statistics. Using Birmingham Clinical Trials Unit's extensive knowledge of delivering Women's Health trials, data collected will be used to model the number of women across the UK likely to be eligible for recruitment into a future RCT **[Core element 1&4: Context, Uncertainties].**

5.5 Work package 4: National Stakeholder event to finalise the C-POP programme theory and recommendations for an effectiveness study (objective 5)

5.5.1 DESIGN

National stakeholder event, guided by PPIE activities and **[Core element 3: Stakeholders].**

5.5.2 TARGET POPULATION

Stakeholders including women as per WP1; HCPs as per WP2; and other stakeholders who might be involved in a future effectiveness study (e.g., (but not limited to) clinical trials units, research and governance teams from potential sites, health economists, HTA representatives, CRNs etc.).

5.5.3 SAMPLE SIZE

Anticipated 30-40 participants.

5.5.4 SAMPLING AND RECRUITMENT

Women and HCPs who participate in WPs 1 and 2 will be invited to take part in the stakeholder event. We will contact them directly using the contact details they provided in WPs 1 and 2. If required, recruitment will be supplemented via the same recruitment pathways identified above in WPs1 and 2 (see sections 5.2.4 and 5.3.4).

Other stakeholders (e.g., health economists, CTU and CRNs) will be identified via professional bodies/membership of societies, adverts on social media, and via the research teams' personal and professional networks and collaborators. Members of our PAG will also be invited.

5.5.5 ELIGIBILITY

(i) Inclusion criteria: Women as per WP1, HCPs as per WP2. Other stakeholders who might be involved in a future effectiveness trial (see above), can converse in English, and who can give informed consent. *(ii) Exclusion criteria:* None. *(iii) Rationale for eligibility criteria:* This sample ensures we have inclusion of a wide range of stakeholders who can provide meaningful insight on our findings and potential future effectiveness trial delivery.

5.6.6 CONSENT

Unless they participated in an earlier interview, participants in the workshop will be asked to complete a short demographic questionnaire to facilitate a description of participant characteristics. All participants in the workshop will complete a consent form prior to the start of the workshop. If the workshop is held remotely, the same pathways will be used as described for WP1 (see section 5.2.6).

5.6.7 DATA COLLECTION

A one day in-person workshop (or remotely if needed), facilitated by the C-POP team and supported by our PPIE group, with discussions (small group and whole group) to encourage interaction between participants. Participants will be given the choice to see the main topics for discussion in advance of their participation, allowing participants to familiarise themselves and raise any queries with the team prior to or during the workshop. At the start of the workshop, we will present our proposed programme theory (revised following WPs 1-3) and initial recommendations for a potential future effectiveness trial. Participants will then be split into smaller discussion groups which will be facilitated by a member of the research team and/or PPIE members. The workshop will offer an opportunity for interaction and communication between participants to provide a non-judgemental and empowering environment where participants feel comfortable and valued enough to share their views and question those of others(53-55).

Discussions will focus on the participants' reflections of the proposed programme theory (see Figure 1) and recommendations for a future effectiveness trial. Views from each group will then be shared and discussed within the whole group with an aim to reach consensus/compromise and ultimately collectively develop the final programme theory, recommendations, and identify future actions following the completion of the C-POP study. Ideally, the workshop will be run face to face in an easily accessible location; however, it is anticipated that given the context of COVID that it may need to be run virtually using a video conferencing platform. This will still allow us to use breakout rooms and employ strategies to ensure everyone feels valued, enhance consensus building and minimise use of resources.

Participants will be offered a £75 voucher to thank them for their time and travel expenses, where appropriate will also be reimbursed.

5.6.7 Data analysis: Discussions will be audio recorded and transcribed. Data generated in the event will be compared to that from WPs1-3 to facilitate collaborative development of the final programme theory and recommendations for a future effectiveness study **[Core element 3-6: Stakeholders, Uncertainties, Refinement and Economics]**.

5.7 End of Study Definition

The end of the study will be defined as the point at which analysis, integration and interpretation of all work packages has been completed and the programme theory for a potential future clinical trial has been finalised. We anticipate this to be in study month 20 (November 2024), where the funding end date is study month 21 (December 2024). REC and the sponsor will be notified of end of study within 90 days of the programme theory being finalised, with a final report due to REC/Sponsor due 12 months after this end of study point. The Draft Final Report to the funder will be submitted within two weeks of the end of the study.

6 Ethical and Regulatory Considerations

6.1 Assessment and Management of Risk

6.1.1 RISK REGISTER

A risk register will be developed maintained by the study management team to assess risk(s) and implement actions to mitigate against or reduce risk(s). Risks will be rated as red (high), amber (medium) or green (low) based on the likelihood that the risk will occur and the potential impact of the risk on the study. The register will be reviewed on a regular basis by the research team as risks (actual and potential) and the associated rating will likely change throughout the study period. The risk register will also be a rolling agenda item for the SMG and SSG meetings. Risks will be categorised into three main sections:

(1) general (e.g., staffing, ethics/governance approvals, subcontracting, COVID-19, resource constraints, time constraints, engagement of recruiters and stakeholders)
(2) participant (e.g., recruitment of sites, identification, diversity of sample, recruitment, sensitivity of discussions, distress, eligibility, disclosure of potential harm, language, availability for interview/events, location of interview/events)
(3) researcher (e.g., sensitivity of discussions, distress, disclosure of harm, location and timing of data collection).

6.1.2 PARTICIPANTS

It is stated in the participant information leaflets, by the person introducing the potential participant to the study, as well as being reiterated by the researcher at the beginning of the interview/event that participants are free to withdraw at any time up to two weeks after the data collection session without having to explain or justify their decision. The welfare of the participants will always be placed ahead of the knowledge to be gained and emotionally distressing topics will be handled with sensitivity and sympathy

and will follow the C-POP Study Distress Pathway (see Appendix 1). The interviewer/event facilitator will also signpost any distressed participant towards services for additional support should this be appropriate (e.g., their secondary care clinician, relevant charities and support services). Information on support services is also provided in the participant information leaflet. We have sought PPIE input to facilitate collaborative design of the study and all participant facing materials to ensure that they are sensitive and suitable for the participant group for this research study.

6.1.3 RESEARCH TEAM

All researchers working within the study (e.g., RFs and SC) will have access to more senior members of the team (e.g., LLJ, CB, SD) to talk through their concerns and decisions made in relation to the study and to reflect on the potentially distressing conversations. A potential risk to the research team is that they may be undertaking interviews in the participants' homes, although the research team is experienced in using this data collection technique. When contacting participants to arrange an interview appointment the researcher will ask the participant about who else will be present during the interview, if there are dogs in the house, whether there is parking etc. If the researcher has concerns, these will be discussed within the research team. Where there are concerns then an informed decision will be made about whether two members of the team attend the interview. If an interpreter will be present for a face-to-face interview (rather than attending the interview via phone) then the researcher will not be by themselves. When interviewing alone, the researcher will also follow their local Lone Worker Policy and will use a buddy system where another member of the research team is contacted upon arrival at the interview location and directly after the end of data collection. The other member of the research team will have access to the location and participant information.

6.2 Research Ethics Committee (REC) and other Regulatory Review/Reports

6.2.1 REGULATORY REVIEW AND COMPLIANCE

The University of Birmingham is the nominated sponsor for this study. Via the Integrated Research Application System (IRAS) system we will seek a favourable opinion from a research ethics committee (REC) the Health Research Authority (HRA) and the required governance and legal compliance approvals. We will seek further local research governance, where required, from each of the Trusts and other Organisations involved in the study (e.g., BSUG, LiveUTIFree). After favourable opinion and commencement of the study, any further substantial amendment[s] will only be implemented following endorsement from the Sponsor, responsible NHS REC and Trusts.

6.2.2 AMENDMENTS

Any amendment[s] to the study will be appropriately notified to the responsible NHS REC by the University of Birmingham, as the Sponsor. The NHS REC will provide a response regarding the amendment[s] within 35 days of receipt of the notice. It will be the Sponsor's responsibility to decide whether an amendment is substantial or non-substantial for the purpose of submission to the NHS REC. Substantial and non-substantial amendment[s], submitted via IRAS, will also be sent to the Research and Development department of each NHS Trust involved in the study to ascertain whether the amendment[s] may affect local NHS permissions. The amendment history will be tracked using version numbers [e.g., 1.0, 2.0] and dates to clearly identify the most recent protocol version.

6.3 Peer Review

The funding application, including the detailed study protocol, has undergone multiple rounds of high quality independent peer review in line with NIHR research funding guidelines. Following the submission of the stage 1 application (outline) we received independent peer review from expert reviewers and the funding board. Following the submission of the stage 2 application (full), we received independent peer review, and further detailed feedback from the funding panel. The study team had the opportunity to respond to both sets of peer review and the feedback from the board. Requested changes were incorporated where appropriate and translated into the current study protocol.

6.4 Patient and Public Involvement

Our collaborative and inclusive approach to patient involvement for this application and proposed study is aligned with the six UK Standards for Public Involvement (56). Within C-POP we have a core PPIE group, involving the CI (LLJ), lead research fellow (EM), PPIE co-applicants (JE and KO'R) and the director of liveUTIfree. The core PPIE group meet ~monthly to support PPIE within C-POP. In addition, we have established a patient advisory group (PAG) that is co-chaired by the PPI lead co-applicants (K'OR and JE) and supported by the CI (LLJ). Our PAG includes a diverse group of women with direct experience of colpocleisis and/or SSF. We have purposively tried to identify and recruit women of different ages, relationship statuses, ethnicities and with different experiences of the condition and surgery. We currently have three PAG members and are working to identify up to a further seven members to increase diversity in terms of culture, ethnicity, and experience of colpocleisis/SSF and to allow a core group to be present for the duration of the study as some participants may drop out/be too unwell to participate.

Based on our PPIE to date, this group of older women are generally technology naïve and even with support find it difficult to engage in group activities (e.g., Zoom). They are geographically disparate and have varying access needs. Therefore, we plan to hold up to four PPIE events at key time points during the study (see Gantt Chart) where members can contribute individually via for example written notes, phone

discussions or via remote meetings (where there are able to). Notes from these engagement periods will be collated by the C-POP team and will be sent to a visual artist who will summarise them. These visual summaries will then be sent to the PAG, and they will be asked to comment in writing/via phone. Further to this, we will present to the Women's Involvement Groups (e.g., BSUG and RCOG) at appropriate time points within the study to seek wider input.

Our patients have contributed to discussions around how we might approach and recruit women (e.g., via clinics where they have a relationship with their clinician), how we should communicate with women (e.g., via phone, physical documents and using visual summaries to facilitate sharing of others views when they have contributed individually), how we might best collect data (e.g., individual interviews) and what are the most important questions for us to ask in the interviews (e.g., consequences of surgery, in particular, around intimacy and the language to use around this particular aspect of the discussion).

Moving forwards, the PAG will collaborate with the team around for example (i) recruitment, by providing advice for optimising participation and developing patient facing information; (ii) data collection and analysis (i.e., JE/KO'R will contribute to interviewing following training by LLJ/CB/EM), via input into content and clarity of interview guides, and involvement in interpretation of the findings; and (iii) dissemination, by working closely with the team to publicise lay friendly outputs. The role and expectations of PPI advisory members have been clearly outlined already and will be formalised (e.g., by providing role descriptors, establishing terms of reference) at the start of the study.

In addition, as part of the study, we plan to hold a national stakeholder event (WP4), including PPIE, following the completion of initial data collection to help provide an opportunity for respondent synthesis, and to provide key design recommendations for an effectiveness trial. If appropriate, the PAG will be asked to attend and contribute to the delivery of this event if they feel able.

Contributions of the PAG will be acknowledged (and co-authored as appropriate) in presentations, reports, and publications. JE/KO'R and the PAG will be involved in writing of a Plain English Summary of the results to facilitate dissemination to a range of audiences. We are also planning to commission a visual artist to develop illustrations of the results and JE/KO'R and the PAG will be involved in the scribe meetings or will be sent physical copies to comment on to ensure that illustrations are acceptable and appropriate to patients. We will monitor and evaluate our PPIE including what has worked well and what we could have done better. We plan to develop an overarching visual summary of our PPIE evaluation to enable sharing and learning within the wider PPIE evidence base. PPI representatives will receive appropriate payment, informed by INVOLVE guidance(57), for their time.

6.5 Summary of patients, service users, carers, public as research participants

Decisions around participant inclusion have been made via our PPIE and informed by the evidence base. For example, we will include all women with A-POP who are eligible for surgery irrespective of their age. We have included four languages in addition to English. Four (English, Polish, Urdu and Punjabi) of the five languages are the most spoken languages in England and Wales, as informed by the 2011 census data(41) and insight from our co-applicants who are practising UG clinicians (AD and PL).

Informed and reviewed as part of our PPIE, the participant facing resources will be designed as accessible for our population group. Qualitative interviews will be offered via several methods (i.e., phone, remote video or face to face) and locations (e.g., clinic, home, safe private space) to ensure that participants, many of which will be older women, have choices regarding engagement and accessibility. WP2 will involve a range of HCPs, including those who work at different types of NHS sites, experience of A-POP surgeries, characteristics of the populations they work with (e.g., areas of high cultural diversity vs areas with high population of older adults), location and geographical spread (e.g., including more than one from England, Wales, Scotland and/or Northern Ireland). We will also gather data from HCPs involved in the surgical and non-surgical care of women with A-POP. In WP3, data will be gathered from an anticipated eight diverse sites across the UK. This will allow us to explore the number of eligible women across different sites which have been sampled for multiple characteristics. In WP4, all participants from WP1 and 2 will be invited to contribute further to the research process by attending the stakeholder event. This ensures ongoing engagement with the study findings which in turn will contribute to and strengthen any future effectiveness trial **[Core element 1&3: Context, Stakeholders]**

6.6 Equality, diversity and inclusion for study participants

We have purposely identified our anticipated recruiting sites to map the diversity of the UK population of women eligible for surgery for their A-POP. This includes sites with a predominantly older population (e.g., Plymouth, Bristol and Cornwall), sites in areas of high cultural diversity (e.g., Birmingham, Coventry), and sites with varying levels of deprivation (e.g., Plymouth, Bristol, Birmingham, Glasgow, Swansea, Sheffield, Shrewsbury, Cornwall, Coventry), those not currently active in research (e.g., Shrewsbury). In addition to English, we will include resources for three of the most spoken languages in the UK: Urdu, Punjabi and Polish, and in Welsh. Our C-POP design aligns with recommendations in NIHR's INCLUDE framework(22), namely identifying and overcoming barriers to recruitment of underserved groups, purposively using NHS site(s) with relevant representation of underserved groups, and applying appropriate eligibility criteria to ensure underserved groups are not excluded **[Core element 1: Context]**.

6.7 Protocol Compliance

Accidental protocol deviations will be adequately documented on the relevant forms and reported to the

Chief Investigator and Sponsor. Serious protocol non-compliance will be reported without delay by research staff to the CI (LLJ) and thence to the study Sponsor and onwards as appropriate. The CI (LLJ) will ensure that the issue is investigated, and appropriate actions taken. The responsible NHS REC will be notified as soon as possible of any serious breach of NHS REC approval conditions, any serious breach of security or confidentiality, or any other incident that could undermine public confidence in the research.

6.8 Data Protection and Patient Confidentiality

All study researchers and clinicians involved in the study will uphold the core principles and comply with the requirements of the Data Protection Act 2018 and the EU General Data Protection Regulation 2016/679 in the collection, storage, processing, and disclosure of personal information. All study researchers and clinicians will also maintain up to date Good Clinical Practice [GCP] training.

The data protection measures of this study will adhere to the relevant policies and procedures of the University of Birmingham. All study data collected on paper will be held securely, in a locked room or locked cabinet that is accessible only to the research team and relevant regulatory authorities. All study data in electronic form will be held on secure networks/encrypted and password protected computers. Consent to contact forms which are completed online will be uploaded via the ReDCAP database at Birmingham Clinical Trials Unit. Audio files will be transcribed by a specialist external company subject to a Confidentiality Agreement/Personal data transfer agreement to not disclose any information to third parties. Files will be transferred via a secure server with user identifiers and passwords. Transcripts will be marked with unique and anonymised identifiers. The interpreter/translation company will also be subject to a Confidentiality Agreement/Personal data transfer agreement. Files will be transferred via a secure server with user identifiers and passwords. All data will be held securely in the custody of the CI (LLJ) for a minimum of 10 years after publication of the main study results, in accordance with the University of Birmingham Research Data Management Policy.

6.9 Indemnity

The University of Birmingham, as the Sponsor, has in force a Public Liability Policy which provides cover for claims for “negligent harm.” The activities of this study are included in the coverage. No provision has been made for indemnity in the event of a claim for non-negligent harm. Insurance and indemnity for NHS staff and participants recruited via NHS sites will be covered by standard NHS indemnity liability arrangements for clinical negligence claims in the NHS.

6.10 Access to the Final Study Dataset

Only the research team, the Sponsors, relevant regulatory authorities, and the funder will have access to the final study dataset that will comprise demographic questionnaires, audio recordings and transcripts of interviews and stakeholder events, and an anonymised database of potentially eligible women for a future trial. After publication of the main findings of the study, the research team will consider external requests to gain access to anonymised data, to be securely shared under the auspices of the CI (LLJ). The dataset will be preserved and available for this purpose for a minimum of 10 years following the end of the study. All requestors wishing to obtain study data will be asked to provide a brief research proposal including the objectives and timelines of the candidate project, intellectual property rights, and expectations for publications and citations. These details will form the basis of a Data Sharing Agreement between the University of Birmingham and the requestor, to clearly establish the responsibilities of each party. It is expected that requestors will, as a minimum, acknowledge the original research team and NIHR funding, and will consider co-authorship of any subsequent publications, if appropriate. Permission for anonymised data to be shared for the purpose of future academic research will be sought from all participants via the informed consent form.

7 Dissemination Policy

7.1 Dissemination Plans

Our dissemination strategy has been informed by NIHR's dissemination and impact guidance(58, 59). We have identified a range of audiences to target for dissemination and impact. These include women with A-POP, people who care for women with A-POP, the public, commissioning organisations (e.g., integrated care systems, NHS England, RCOG), healthcare and social care professionals involved in UG service provision, external statutory organisations (e.g., Department for Health and Social Care, NICE, NHS Information Centres, BSUG), and other organisations (e.g., Bladder Health UK, liveUTIfree). Our dissemination strategy will target the breadth of these audiences. Our strategy will be developed using evidence for translating knowledge into practice, for example, the Scientist Knowledge Translation Plan(60, 61) and the NIHR dissemination and impact guidance(58). We will prioritise early dissemination using a proactive strategy to maximise the likelihood of reaching key audiences and furthering public and academic knowledge around surgical interventions for AP. Although all members of the project team will have a role in dissemination, several members of our team will be able to act as dissemination champions (i.e., study coordinator (TBC), CI (LLJ), PPIE leads (JE and KO'R), and practising clinicians (AD and PL)). We will use various methods to inform stakeholders of our work, including:

- **Early stage and ongoing methods**: blogs, social media outputs, infographics aimed at different audiences and ongoing networking with stakeholders such as BSUG etc.

- **End of study methods**: published articles, NIHR report (threaded publication), conference presentations (e.g., International Continence Society Conference; IUGA Annual meeting, BSUG scientific update), press release of study findings, end of study video summary.

To ensure that dissemination is not solely passive, we will include active strategies. For example, we are fortunate that our co-applicant patient representative (JE) is the only patient advocate on the National Bladder and Bowel Project(62) and the NHS England Excellence in Continence Care Board(63). Several members of the team are representatives on the All Party Parliamentary Group Bladder and Bowel Care(64). Our other co-applicant patient representative (KO'R) is the Patient and Public Involvement lead for ROCG. Further to this, we have active support from RCOG, BSUG research network and liveUTIfree via their Women's Voices Involvement Panels and contacts with practising clinicians to support dissemination activities. As a team, and with our wider networks, we are therefore in a unique position to disseminate the emerging and final recommendations, and activity discuss them, with these key groups **[Core element 3: Stakeholders].**

7.1.1 PROPOSED KEY OUTPUTS

Study findings will be owned by the University of Birmingham as per the funding contract and collaboration agreement. The PAG will contribute to the dissemination plan. The level of dissemination will be in keeping with that appropriate for a multi method (predominantly qualitative) research study. Our dissemination strategy has been informed by NIHR's dissemination and impact guidance(58, 59). We plan to proactively disseminate and engage with our key audiences from the outset of the project. Our audiences include women with AP, people who care for women with AP, the public, commissioning organisations, HCPs involved in care provision, external statutory organisations, and third sector condition specific organisations. We will use a range of tailored dissemination strategies to target our audiences, including:

(i) a final programme theory demonstrating the considerations for feasibility and acceptability of a future trial

(ii) academic publication of our findings in peer-reviewed journal(s), including a published report in the NIHR journals library

(iii) presentation of our findings at academic and/or HCP conferences

(iv) recommendations for future clinical and policy revision

(v) press releases of our study start up and study findings

(vi) 'at a glance' visual summaries, infographics and blog articles

(vii) physical participant newsletter leaflets

(viii) short engaging video(s) for online dissemination, created for accessibility with appropriate closed caption subtitles

(ix) dissemination of our outputs via a study website.

We will also host:

(i) a study website providing updates on the study

(ii) an active Twitter account as a method of disseminating information to public, academia and HCPs

(iii) webinars to inform stakeholders of our, findings and/or future steps

Please note that the timing and content of the outputs may be dependent on whether a future trial is feasible. We will need to be mindful of the potential impact that sharing such information publicly might have on ability to recruit sites and randomise participants in any future trial.

7.2 Anticipated Outcomes and Impact

A key output will be the C-POP programme theory. Future research will build on aspects of the programme theory to, in the longer term, create guidelines and recommendations for surgical management of A-POP. As identified by the MRC/NIHR Framework for Developing and Evaluating Complex Interventions(36), development, testing and refining programme theory is a core element of evidence generation. This allows our research team, and future researchers and decision makers, to build on the knowledge gained from C-POP to ultimately improve decision making for A-POP surgical procedures.

Our outputs have the potential to inform current and future health service strategies. For example, C-POP aligns with the NHS's pelvic health initiative being piloted over 14 NHS trusts, which aims to "*improve the prevention, identification and treatment of pelvic floor dysfunction, so that fewer women experience ongoing issues after giving birth and later in life*"(65).

Overall, our combination of proposed outputs and outcomes have the potential to generate better information for women and HCPs about how to make informed (surgical) treatment choices. This may be in the form of HCP training, HCP guidelines, patient information resources, and general awareness raising which in turn feeds into public discourse about AP and its management.

7.3 Authorship Eligibility Guidelines

A publication plan will be agreed, supported by the funder, in the second year of the project which will specify the planned publications, including authorship. Individual contributions to the study will be reviewed with consideration for the authorship criteria of the International Committee of Medical Journal Editors [ICMJE], to determine authorship of any manuscript[s] submitted for publication.

8 References

1. Primary Care Women's Health Forum. What is the cost of pelvic organ prolapse to the NHS? 2019 [Available from: https://pcwhf.co.uk/news/what-is-the-cost-of-pelvic-organ-prolapse-to-the-nhs/.
2. Ibrahim S, McPherson K, Hagen S, Cooper K, Guerero K, Agur W. BSUG Survey of the Management of Pelvic Organ Prolapse in the Elderly, Sexually-inactive Women. icsorg. 2017.
3. National Institute for Health and Care Excellence. Urinary incontinence and pelvic organ prolapse in women: management [NG123] 2019 [Available from: https://www.nice.org.uk/guidance/ng123/chapter/Context.
4. Murphy AM, Clark CB, Denisenko AA, D'Amico MJ, Vasavada SP. Surgical management of vaginal prolapse: current surgical concepts. Can J Urol. 2021;28(S2):22-6.
5. British Society for Urogynaecology (BSUG). Vaginal vault suspension surgery in the UK 2008-2017: Sacrospinous fixation. 2019.
6. British Society for Urogynaecology (BSUG). Colpocleisis data 2019-2022. 2022.
7. Grzybowska ME, Futyma K, Kusiak A, Wydra DG. Colpocleisis as an obliterative surgery for pelvic organ prolapse: is it still a viable option in the twenty-first century? Narrative review. Int Urogynecol J. 2022;33(1):31-46.
8. Krissi H, Aviram A, Ram E, Eitan R, Wiznitzer A, Peled Y. Colpocleisis surgery in women over 80 years old with severe triple compartment pelvic organ prolapse. Eur J Obstet Gynecol Reprod Biol. 2015;195:206-9.
9. Mueller MG, Ellimootil C, Abernethy MG, Mueller ER, Hohmann S, Kenton K. Colpocleisis: a safe, minimally invasive option for pelvic organ prolapse. Female Pelvic Medicine & Reconstructive Surgery. 2015;21(1):30-3.
10. Greisen S, Axelsen SM, Bek KM, Guldberg R, Glavind-Kristensen M. Fast track sacrospinous ligament fixation: subjective and objective outcomes at 6 months. BMC Womens Health. 2021;21(1):154.
11. Mothes AR, Wanzke L, Radosa MP, Runnebaum IB. Bilateral minimal tension sacrospinous fixation in pelvic organ prolapse: an observational study. Eur J Obstet Gynecol Reprod Biol. 2015;188:1-5.
12. Flynn BJ, Webster GD. Surgical management of the apical vaginal defect. Curr Opin Urol. 2002;12(4):353-8.
13. Melon J. A commentary on "A qualitative study of women's values and decision-making surrounding LeFort colpocleisis". Int Urogynecol J. 2020;31(6):1105.
14. Yalcin Y, Demir Caltekin M, Eris Yalcin S. Quality of life and sexuality after bilateral sacrospinous fixation with vaginal hysterectomy for treatment of primary pelvic organ prolapse. Low Urin Tract Symptoms. 2020;12(3):206-10.
15. Deval B. Hysterocolpectomy with colpocleisis for massive genital prolapse in women aged over 70 years. Eur J Obstet Gynecol Reprod Biol. 2005;123(2):249-53.
16. Wang YT, Zhang K, Yang JF, Yao Y, Wang HF, Han JS. Sexually Inactive Status in Women With Pelvic Organ Prolapse Before Colpocleisis and Postoperative Satisfaction and Regret Rate. Female Pelvic Med Reconstr Surg. 2021;27(9):556-9.
17. FitzGerald MP, Brubaker L. Colpocleisis and urinary incontinence. Am J Obstet Gynecol. 2003;189(5):1241-4.
18. Salant T, Lauderdale DS. Measuring culture: a critical review of acculturation and health in Asian immigrant populations. Soc Sci Med. 2003;57(1):71-90.
19. Arousell J, Carlbom A. Culture and religious beliefs in relation to reproductive health. Best Pract Res Clin Obstet Gynaecol. 2016;32:77-87.

20. Department of Health. Religion or belief: A practical guide for the NHS. 2009.
21. Goode PS, Fitzgerald MP, Richter HE, Whitehead WE, Nygaard I, Wren PA, et al. Enhancing participation of older women in surgical trials. J Am Coll Surg. 2008;207(3):303-11.
22. National Institute for Health Research (NIHR). Improving inclusion of under-served groups in clinical research: Guidance from the NIHR-INCLUDE project. 2020.
23. National Institute for Health Research (NIHR). Health Inequalities Assessment Toolkit. Lancaster, UK; 2017.
24. Lu M, Zeng W, Ju R, Li S, Yang X. Long-Term Clinical Outcomes, Recurrence, Satisfaction, and Regret After Total Colpocleisis With Concomitant Vaginal Hysterectomy: A Retrospective Single-Center Study. Female Pelvic Medicine & Reconstructive Surgery. 2020.
25. Wang YT, Zhang K, Wang HF, Yang JF, Ying Y, Han JS. Long-term efficacy and patient satisfaction of Le Fort colpocleisis for the treatment of severe pelvic organ prolapse. Int Urogynecol J. 2021;32(4):879-84.
26. Favre-Inhofer A, Carbonnel M, Murtada R, Revaux A, Asmar J, Ayoubi JM. Sacrospinous ligament fixation: medium and long-term anatomical results, functional and quality of life results. BMC Womens Health. 2021;21(1):66.
27. Ertas IE, Balıkoğlu M, Biler A. Le Fort colpocleisis: An evaluation of results and quality of life at intermediate-term follow-up. J Gynecol Obstet Hum Reprod. 2021;50(4):102069.
28. Catanzarite T, Rambachan A, Mueller MG, Pilecki MA, Kim JY, Kenton K. Risk factors for 30-day perioperative complications after Le Fort colpocleisis. J Urol. 2014;192(3):788-92.
29. Villot A, Pizzoferrato AC, Longie A, Paniel BJ, Fauconnier A. Technical considerations and mid-term follow-up after vaginal hysterocolpectomy with colpocleisis for pelvic organ prolapse. Eur J Obstet Gynecol Reprod Biol. 2020;247:73-9.
30. FitzGerald MP, Richter HE, Siddique S, Thompson P, Zyczynski H. Colpocleisis: a review. Int Urogynecol J Pelvic Floor Dysfunct. 2006;17(3):261-71.
31. Royal College of Obstetricians and Gynaecologists (RCOG). Better for Women: Improving the health and wellbeing of girls and women. 2019.
32. Recommendations | Urinary incontinence and pelvic organ prolapse in women: management | Guidance | NICE [
33. Digesu GA, Chaliha C, Salvatore S, Hutchings A, Khullar V. The relationship of vaginal prolapse severity to symptoms and quality of life. BJOG. 2005;112(7):971-6.
34. Glazener C, Breeman S, Elders A, Hemming C, Cooper K, Freeman R, et al. Clinical effectiveness and cost-effectiveness of surgical options for the management of anterior and/or posterior vaginal wall prolapse: two randomised controlled trials within a comprehensive cohort study - results from the PROSPECT Study. Health Technol Assess. 2016;20(95):1-452.
35. Olsen AL, Smith VJ, Bergstrom JO, Colling JC, Clark AL. Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol. 1997;89(4):501-6.
36. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. BMJ. 2021;374:n2061.
37. Skivington K, Matthews L, Simpson SA, Craig P, Baird J, Blazeby JM, et al. Development of the framework. HEALTH TECHNOLOGY ASSESSMENT. 2021;25(57):1-+.
38. Funnell S RP. Purposeful program theory: Effective use of theories of change and logic models. 1st ed:

Jossey-Bass; 2011.

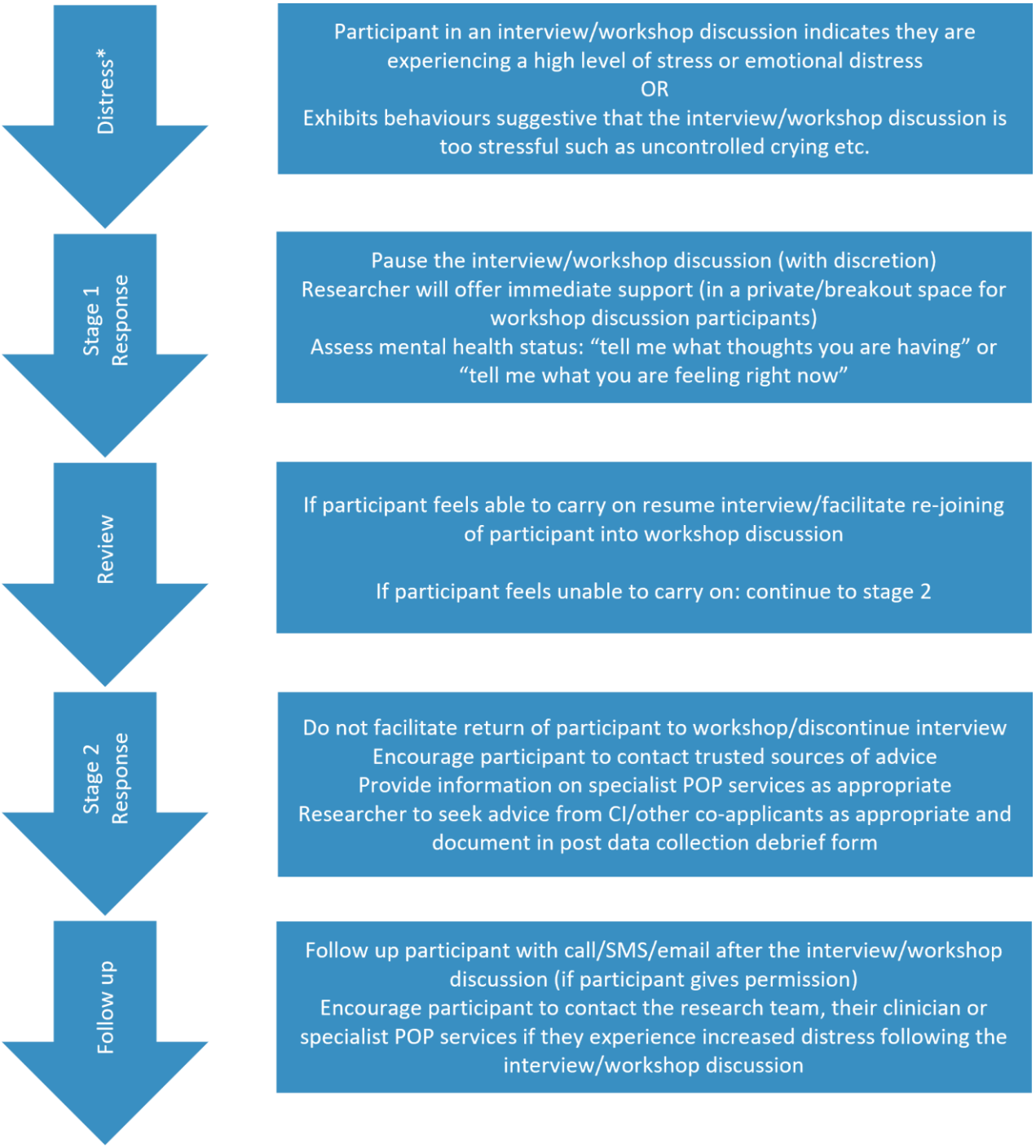
39. Lawless A, Baum F, Delany-Crowe T, MacDougall C, Williams C, McDermott D, et al. Developing a Framework for a Program Theory-Based Approach to Evaluating Policy Processes and Outcomes: Health in All Policies in South Australia. Int J Health Policy Manag. 2018;7(6):510-21.
40. Malterud K, Siersma VD, Guassora AD. Sample Size in Qualitative Interview Studies: Guided by Information Power. Qual Health Res. 2016;26(13):1753-60.
41. Office for National Statistics. Home People, population and community Cultural identity Language Language in England and Wales Language in England and Wales: 2011 2013 [Available from: https://www.ons.gov.uk/peoplepopulationandcommunity/culturalidentity/language/articles/languageinenglandandwales/2013-03-04#:~:text=In%20the%202011%20Census%2C%2092.3,main%20language%20other%20than%20English.
42. Ritchie J, Lewis J. Qualitative research practice: a guide for social science students and researchers. London: Sage; 2003.
43. Braun V, Clarke V. Successful qualitative research: a practical guide for beginners. Thousand Oaks, CA: Sage; 2013.
44. Chun Tie Y, Birks M, Francis K. Grounded theory research: A design framework for novice researchers. SAGE Open Med. 2019;7:2050312118822927.
45. Draucker CB, Martsolf DS, Poole C. Developing distress protocols for research on sensitive topics. Arch Psychiatr Nurs. 2009;23(5):343-50.
46. Montgomery P, Bailey PH. Field notes and theoretical memos in grounded theory. West J Nurs Res. 2007;29(1):65-79.
47. Al-Amer R, Ramjan L, Glew P, Darwish M, Salamonson Y. Translation of interviews from a source language to a target language: examining issues in cross-cultural health care research. J Clin Nurs. 2015;24(9-10):1151-62.
48. Squires A. Methodological challenges in cross-language qualitative research: a research review. Int J Nurs Stud. 2009;46(2):277-87.
49. Dempsey L, Dowling M, Larkin P, Murphy K. Sensitive Interviewing in Qualitative Research. Res Nurs Health. 2016;39(6):480-90.
50. Santos HP, Jr., Black AM, Sandelowski M. Timing of translation in cross-language qualitative research. Qual Health Res. 2015;25(1):134-44.
51. Braun V, V. C. Thematic Analysis: A Practical Guide London SAGE Publications 2021.
52. Carter N, Bryant-Lukosius D, DiCenso A, Blythe J, Neville AJ. The use of triangulation in qualitative research. Oncol Nurs Forum. 2014;41(5):545-7.
53. Freeman T. 'Best practice' in focus group research: making sense of different views. J Adv Nurs. 2006;56(5):491-7.
54. Kitzinger J. Qualitative research. Introducing focus groups. BMJ. 1995;311(7000):299-302.
55. Krueger R, Casery M. . Focus Groups: A Practical Guide for Applied Research. Thousand Oaks, CA: Sage; 2015.
56. National Institute for Health Research. UK Standards for Public Involvement 2020 [Available from: https://sites.google.com/nihr.ac.uk/pi-standards/standards?authuser=0.
57. National Institute for Health Research. Policy on payment of fees and expenses for members of the public actively involved with INVOLVE 2016 [Available from: https://www.invo.org.uk/wp-

content/uploads/2016/05/INVOLVE-internal-payment-policy-2016-final-1.pdf.

58. National Institute for Health and Care Excellence. How to disseminate your research: NIHR; 2019 [Available from: https://www.nihr.ac.uk/documents/how-to-disseminate-your-research/19951.
59. National Institute for Health and Care Excellence. Plan your pathway to impact: NIHR; 2022 [Available from: https://www.nihr.ac.uk/researchers/apply-for-funding/how-to-apply-for-project-funding/plan-for-impact.htm.
60. Barwick M. Building Scientist Capacity in Knowledge Translation: Development of the Knowledge Translation Planning Template. Technol Innov Manag Rev. 2016;6(9):9-15.
61. Barwick M. Knowledge Translation Planning Template. Ontario: The Hospital for Sick Children; 2017 [Available from: http://www.sickkids.ca/pdfs/Learning/79482-KTPlanningTemplate.pdf.
62. NHS Supply Chain. National Bladder and Bowel Health Project [Available from: https://www.supplychain.nhs.uk/programmes/national-bladder-and-bowel-health-project/.
63. NHS England. Excellence in Continence Care: Practical guidance for commissioners, and leaders in health and social care 2018 [Available from: https://www.england.nhs.uk/wp-content/uploads/2018/07/excellence-in-continence-care.pdf.
64. APPG for Bladder and Bowel Continence Care. All Party Parlimentary Group for Bladder and Bowel Continence Care 2020 [Available from: http://www.appgcontinence.org.uk/.
65. NHS England. NHS pelvic health clinics to help tens of thousands of women across the country: NHS England; 2021 [Available from: https://www.england.nhs.uk/2021/06/nhs-pelvic-health-clinics-to-help-tens-of-thousands-women-across-the-country/
66. Draucker C, Martsolf, D., Poole, C. Developing distress protocols for research on sensitive topics. Archives of Psychiatric Nursing. 2009;23(5):343-50.

9 Appendices

9.1 Appendix 1 C-POP Study Distress Pathway



*Protocol for managing distress in the context of research on senstitive topics (Adapted from:(66))