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Research Protocol

Full title of project: A Patient-reported outcome measure for PRolApse, Incontinence and meSh complication surgEry: The APPRAISE study

Research Protocol Version:	**V 1.0**
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Contents

List of Abbreviations

APPRAISE	A Patient-reported outcome measure for PRoLApse and mesh complication surgery
BPS	British Psychological Society
BMC	BioMed Central Journal
BSUG	The British Society of Urogynaecology
BSUG RN	The British Society of Urogynaecology Research Network
CENTRAL	Cochrane Central Register of Controlled Trials
CFA	Confirmatory factor analysis
COMET	Core Outcome Measures in Effectiveness Trials
CoP	Community of Practice
COS	Core outcome set
COSMIN	COnsensus-based Standards for the Selection of Health Measurement Instruments
DCE	Discreet choice experiments
EQ-5D	EuroQol instruments
FDA	U.S. Food and Drug Administration
GRIPP	Guidance for Reporting Involvement of Patients and the Public
HRA	Health Research Authority (NHS)
HSDR	Health and Social Care Delivery Research (HSDR)
HTA	Health technology assessment
IHO	Inspired Health Outcomes
ISOQOL	International Society of Quality of Life Research
KMO	Kaiser-Meyer-Olkin Test
LBU	Leeds Beckett University
NHS	National Health Service (UK)

NIHR	National Institute for Health and Care Research
NICE	National Institute for Health and Care Excellence
PBM	Preference based measure
PIL	Participant information leaflet
POP	Pelvic organ prolapse
POP SS	Pelvic Organ Prolapse Symptom Score
PPI	Patient and Public Involvement
PREM	Patient-reported experience measure
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PROM	Patient-reported outcome measure
PROSPECT	PROlapse Surgery: Pragmatic Evaluation and randomised Controlled Trials (University of Aberdeen)
PROSPERO	International prospective register of systematic reviews (University of York)
PURSUE	People with URogynacological conditions: Understanding Experiences (University of Oxford)
QALYs	Quality adjusted life years
QoL	Quality of life
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomised control trial
ScHARR	School of Health and Related Research (University of Sheffield)
SUI	Stress urinary incontinence
TA	Translatability assessment
WP	Work package

1. Project Details

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1.2 Sponsor Details

Leeds Beckett University

1.3 Title of the Project

Full title: A Patient-reported outcome measure for PRolApse, Incontinence and meSh complication surgEry.
Short title: The APPRAISE Study

1.4 Funders Reference Number

NIHR152187

1.5 Protocol Version Number and Date

V1.0, 1ST May 2023

1.6 Research Question

Is a new patient-reported outcome measure to assess surgical interventions for pelvic organ prolapse, stress urinary incontinence and mesh complications a reliable measure and acceptable for use in clinical trials and other evaluation studies?

2. Scientific Abstract

Background: Different surgical treatments are available to treat pelvic organ prolapse (POP) and stress urinary incontinence (SUI); some use polypropylene mesh which has led to complications requiring further corrective surgery.[1] This has negatively impacted upon women's[1] experiences of using urogynaecology services and seeking treatment for these conditions. However, there is currently no surgical intervention-specific patient-reported outcome measure (PROM) available for these women to tell us about these harmful effects. As a result, evidence is missing on which are the best treatments and their risks and complications[2], in part because of inadequacies in understanding the full range of experiences of previous patients. NICE have highlighted the need for a single PROM specific for pelvic floor surgery to be developed and validated to support further research into the best treatment decisions, with cross-cultural applicability.[2]

Aim: To develop a psychometrically validated PROM to compare outcomes for the different surgical approaches to treat POP, SUI and mesh complications that captures the full range of effects on quality of life (QoL), including patient experience, and long-term complications, which can also be used in economic evaluations. An assessment of barriers and facilitators to its implementation and use as an outcome measure in clinical effectiveness studies will also be undertaken.

Timeframe: Three years

Setting: NHS secondary care urogynaecology services and the Sheffield Mesh Removal Centre (Group 3). Recruitment Centres include ethnically and geographically diverse populations (urban, inner city, coastal, rural) across, Sheffield, Norfolk, Surrey and London. The British Society of Urogynaecology Research Network (BSUG RN) includes a further 21 secondary care units which are UK wide and will also recruit patients into this study.

Target population: Group 1: Women aged 16 years or over who have undergone surgical intervention for POP. The surgical interventions include the mesh procedure or its alternatives (vaginal hysterectomy + vaginal wall repair, sacrospinous fixation + vaginal wall repair, Manchester repair, sacrospinous hysteropexy, abdominal or perineal surgery to treat a rectal prolapse). Group 2: Women aged 16 or over who have undergone surgical intervention for SUI. The surgical interventions include mesh or its alternatives (colposuspension, autologous fascial sling, urethral bulking). Group 3: Women aged 16 or over with mesh complications arising from surgical treatment for POP and SUI who have undergone surgery.

Inclusion/Exclusion Criteria: Women will be included if they have undergone surgery for POP, SUI or mesh complications but excluded if they are under 16 years old.

Design and Theoretical/Conceptual Framework: A mixed methods sequential design across six work packages (WP), consistent with the FDA guidance for developing PROMs[3], fulfilling the standards outlined by the International Society of Quality-of-Life Research (ISOQOL)[4] and the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN).[5-6]

Methods: In WP1 we will undertake a systematic review of reviews to identify what existing PROMs and PREMs items and domains are relevant to measure surgical outcomes for POP, SUI and mesh complications. We will also undertake a qualitative evidence synthesis to understand women's self-reported experiences following these surgical interventions. This synthesis will include the findings from the PURSUE study (NIHR202450) which recently interviewed 75 people using urogynaecology services. We will build on this evidence base by gathering direct patient input from 20-25 concept

[1] Within this document we use the term women and women's health. However, it is important to acknowledge that it is not only people who identify as women for whom it is necessary to access care. Obstetric and gynaecology services and delivery of care must therefore be appropriate, inclusive and sensitive to the needs of those individuals whose gender identity does not align with the sex they were assigned at birth and we would be respectful of this throughout the delivery of this project and in the resulting PROM.

elicitation interviews with women from our three target groups to ensure the content validity of the PROM. We will also explore preferences for PROM format and potential implementation challenges. We will then produce the first prototype of the questionnaire in paper and electronic formats. In WP2 we undertake a stakeholder meeting to review the initial content of the PROM and perform 30 cognitive interviews with women as they are completing the questionnaire to ascertain how acceptable it is to them. We will also undertake a translatability assessment exercise to ensure that our PROM can be easily translated into other languages, inviting 12 women back from the cognitive interviews to check if any changes made are still acceptable. Next, in WP3, we will undertake a postal survey with 250 women to reduce the number of items and identify the domain structure and scoring algorithms of the PROM. This will be followed by a second survey in a new sample of 300 women to confirm the domain structure, and establish the reliability, validity and responsiveness of the tool in the context of short-term surgical outcomes up to 6 months post-treatment. In WP4, another survey will be undertaken with a new sample of 300 women to establish the psychometric properties of the tool in the context of long-term surgical outcomes, between 6 months and 10 years post-surgery. We will also administer the PROM to 400 women who are between 12-14 years post-surgery recruited from the follow-up PROSPECT Study to assess the PROMs psychometric properties in the context of a clinical trial. In WP5, we will develop a preference-based version of the PROM enabling the calculation of quality adjusted life years (QALYs) for use in future cost-effectiveness studies. Finally, in WP6, we will interview NHS staff and trialists to identify and solve any possible barriers to its utility. The PROM will be co-developed with patient involvement throughout study delivery in partnership with the Sheffield Reproductive Health Research Public Advisory Panel, a woman with experience of mesh harm, and the Women's Voices of the Royal College of Obstetricians and Gynaecologists (RCOG).
Dissemination and Impact: To embed our outputs in future practice we will disseminate with support from professional societies (e.g., BSUG, British Association of Urological Surgeons and the Pelvic Floor Society) and present our findings across social and mainstream media outlets, at healthcare conferences, in leading academic journals and with relevant third sector parties. At the end of the study, we will produce the psychometrically robust APPRAISE PROM in plain English language in paper and electronic formats, a YouTube video and visual aids to share the findings with patients and the public, and a user manual targeted at healthcare professionals to support use in clinical effectiveness studies. Later, our concept elaboration document will facilitate easy translation of the PROM into other languages, and NHS Digital will also adopt the PROM and field test it in the National Registries and with women taking part in clinical trials.

3. Background and Rationale

A literature search of PROSPERO and the Cochrane Library (including the CENTRAL trials register) using search terms "pelvic organ prolapse", "stress urinary incontinence", "mesh", "surgery OR surgical" informed this section. Different surgical treatments are available for POP and SUI; some use polypropylene mesh which has led to complications requiring further corrective surgery.[1] Evidence is missing on which are the best treatments and their risks and complications[2], in part because of inadequacies in understanding the full range of experiences of previous patients. The National Institute for Health and Care Excellence (NICE) have highlighted the need for a single patient-reported outcome measure (PROM) specific for pelvic floor surgery to be developed and validated to support further research into the best treatment decisions, with cross-cultural applicability.[2]

Pelvic floor disorders, including pelvic organ prolapse (POP) and stress urinary incontinence (SUI), inflict a substantial burden on women, their families, healthcare providers and society. Yet it remains unclear what are the optimal treatments for these conditions.[7] Despite data on the success rates of surgical procedures[2], the evidence for subsequent adverse effects and risks is limited.[8] Whether as a

first treatment or undergoing corrective mesh removal surgery, there is no standardised means of collecting patient-reported outcomes, so it remains unclear what the impacts of these surgical treatments are. Numerous systematic reviews have already synthesised the existing PROMs suitable for use in women with pelvic floor disorders[9-13], including by our study team members.[9-10] However, these existing tools all predate the U.S. Food and Drug Administration (FDA) framework for developing PROMs and lack the methodological rigour now required to inform clinical effectiveness. Other systematic reviews have already proposed interim core outcome sets (COS) in POP and SUI surgery trials[14-15] also including a team member (SD). Hence, we will undertake a review of these reviews; seeking to include relevant systematic reviews currently in progress.[16] There are qualitative evidence syntheses to understand women's experiences of living with POP and SUI[17-18], but none are procedure-specific. We will address this. There are over 85 PROMs assessing pelvic floor symptoms in women undergoing pelvic floor surgery.[10] However, they have been criticised because they tend to focus on symptoms exclusively related to the clinical problem rather than capturing broader issues related to quality of life (QoL) for patients. In addition, there is no PROM designed specifically to assess surgical outcomes for women undergoing surgery for mesh complications.[2,10]

Consequently, there is an urgent need for a single universally accepted PROM, linked to the surgical registry established by NHS England. This would generate sufficiently large datasets to answer pressing research questions relating to the efficacy of the surgical treatments, short- and long-term outcomes and differences between these interventions as self-reported by women. This aligns with the goals of the new Women's Health Strategy for England[19] to increase understanding of pelvic floor health conditions and address a data disparity by having a robust surgery-specific PROM to identify what treatments work best for women.

4. Aims and Objectives of the Study

4.1 Aim

The aim of this research is to develop and validate a PROM (including patient experience) for use in clinical effectiveness studies (including clinical trials, routine care, registries, and service evaluation) with a diverse sample of patients who have undergone surgical treatment for POP, SUI or mesh complications.

4.1 Objectives

Reflecting the project's six work-packages (WP), we will:

1. Review the literature and gather qualitative evidence to inform the PROM's theoretical basis and content, including its conceptual framework, items and response format (WP1).
2. Conduct a cognitive interviewing exercise and translatability assessment to ensure the PROM is acceptable to users and has cross-cultural applicability (WP2).
3. Administer the PROM in two patient surveys to establish its psychometric properties in the context of short-term surgical outcomes up to 6 months post-surgery (WP3).
4. Administer the PROM in two patient surveys to establish its psychometrics in the context of long-term surgical outcomes beyond 6 months post treatment, and in the context of a clinical trial (WP4).
5. Develop a preference-based version of the PROM enabling the calculation of quality adjusted life years (QALYs) from PROM data (WP5).
6. Gather qualitative evidence to understand what may inhibit or facilitate use of the PROM in clinical effectiveness studies (WP6).

5. Design and Theoretical/Conceptual Framework

The development and evaluation of the new PROM will utilise a mixed-method design, consistent with FDA guidance for developing PROMS.[3] This work will be completed in six work packages to ensure that the final measure fulfils the standards outlined by the International Society of Quality-of-Life Research (ISOQOL)[4], and the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN).[5-6]

5.1 Health Technologies Being Assessed

As the purpose of the PROM is to evaluate surgical interventions, it will be developed and evaluated in the context of clinical effectiveness studies. Preference weights will be derived to generate quality adjusted life years (QALYs) to inform cost-per-QALY analyses in future studies.

5.2 Timeframe

Our programme of work will be completed in three years.

5.3 Patient Population

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Group 1: Women aged 16 years or over who have undergone surgical intervention for POP. The surgical interventions include the mesh procedure or its alternatives (vaginal hysterectomy + vaginal wall repair, sacrospinous fixation + vaginal wall repair, Manchester repair, sacrospinous hysteropexy, abdominal or perineal surgery to treat a rectal prolapse).

Group 2: Women aged 16 years or over who have undergone surgical intervention for SUI. The surgical interventions include mesh or its alternatives (colposuspension, autologous fascial sling, urethral bulking).

Group 3: Women aged 16 years or over who have undergone surgery for mesh complications.

5.4 Inclusion/Exclusion Criteria

Women will be included if they have undergone surgery for SUI, POP or mesh complications but excluded if they are under 16 years old.

5.5 Participant Support

A website will provide information about the study and its aims/objectives. Updates will also be provided via social media. There will be a participant helpline to the research team and an email address for support. Every participant will receive a study debrief form, as recommended by the British Psychological Society (BPS). It explains the aims and expected outcomes of the research, signpost them to free sources of support, and reminds of their rights for data withdrawal and how this may be achieved. This will be supported by our patient information leaflet (PIL) and we have asked for funding to translate our study recruitment documentation into four languages for women who might prefer to read in their first language. Patients will also have access to their urogynaecology nurses should they wish to discuss concerns regarding surgery.

5.6 Setting/Context

NHS secondary care urogynaecology services (Groups 1 and 2) and the Sheffield Mesh Removal Centre (Group 3).

5.7 Recruitment and Consent

Our core recruitment centres include ethnically and geographically diverse populations (inner city, coastal, rural) across, Sheffield, Norfolk, Surrey and London. Approximately 200-300 women per year undergo POP surgery in each centre (up to 1200 women in total per year), and 50 women per year undergo surgery for SUI (up to 200 in total per year). Approximately 50 women per year undergo mesh removal at the Sheffield Mesh Removal Centre. Clinical team members will act as patient identification centres and facilitate recruitment of women with different characteristics using existing databases of operation notes and approaching women attending for outpatient appointments post-surgery. We also have access to a further 21 UK-wide secondary care urogynaecology units via the The British Society of Urogynaecology Research Network (BSUG RN) who will support recruitment to ensure sample diversity. All participant facing materials will be co-developed with PPI input and written in plain English language with a Flesch reading age of 11 years old.

5.8 Equality, Diversity and Inclusivity

Maximising recruitment from geographically (urban, inner city, coastal and rural) and ethnically diverse groups has been given much priority. Recruitment in Sheffield and London provides access to exceptionally ethnically diverse populations (e.g., 19% of Sheffield's population is from black or minority ethnic groups) with many recent migrant groups across these locations too (e.g., Somali, Yemeni, Roma). Building on the expertise of successful outreach services, we will ensure ethnic diversity in all WPs, facilitating participation by including the virtual interpreting phone services (which caters for most languages), and providing interpreters and translated materials (for which funding has been requested). We will encourage participation diversity in disability and gender status via our information leaflets, the study website and social media accounts. We have the support of the BSUG RN to widen recruitment across 21 UK wide sites to ensure these patients are represented throughout our study. Our patient and public involvement (PPI) panel target has 50% representation from hard-to-reach groups. We will also offer patients the opportunity to complete either a paper-based version or electronic version of the PROM (Qualtrics) to ensure that issues around internet access and or factors that might limit ability to engage with a postal survey are reduced. Additional information is provided about our sample, sample size and recruitment methods in each individual work package where relevant.

5.9 Outcome Data

5.9.1 Shorter-Term Surgical Outcome Data

PROM data will be collected in WP3 before surgery, 3 months and 6 months post-surgery. The utility-based algorithm will enable costs per QALY to be calculated.

5.9.2 Longer-Term Surgical Outcome Data

PROM data will be collected in WP4a from women between 6 months and 10 years post-surgery using existing operating theatre system databases. Long-term surgical outcome data in the context of a

clinical trial will also be collected in WP4b in collaboration with the PROSPECT follow-up study (NIHR133665)20 who have kindly agreed to administer our PROM to facilitate its psychometric testing in this context. This cohort of women will be at least 12-14 years post-surgery.

5.10 Measurement of Costs and Outcomes

We will not be calculating the cost per QALY, in this study. However, we will be generating a preference-based version of our PROM that enables the generation of QALYs in retrospective and prospective datasets and these can then be used to inform cost-per-QALY analyses in future studies. In pelvic floor medicine and surgery there are no established core outcome sets currently available. However, co-applicant SD is part of the iChorus team working with the COMET initiative towards the development of core outcome sets. Their interim core outcome sets in SUI and POP surgical trials will be taken into consideration when developing the PROM.[13-14]

PLAN OF INVESTIGATION

6. WP1 (Months 1-11)

To develop the conceptual framework and ensure the content validity of the PROM, we will undertake two systematic reviews (1a & 1b), a secondary data analysis of a subset of PURSUE study (NIHR 202450) interviews (1c) and undertake concept elicitation interviews, informed by the findings generated from the PURSUE Study (1d). Protocols for both systematic reviews will be registered on PROSPERO.

6.1 Systematic Review (1a): A Systematic Review of Reviews

6.1.1 Aim

To identify what existing PROMs and patient-reported experience measures (PREMs), items, domains, recall periods and response options are relevant to measure surgical outcomes for POP, SUI and mesh complications.

6.1.2 Method

A systematic review of reviews based on JBI methodological guidance from on umbrella reviews, and systematic reviews of measurement properties.[21-23]

6.1.3 Review Questions

1. What PROMs, PREMs, items, domains, recall periods and response options have been used to measure surgical outcomes for POP, SUI and mesh complications in studies included in systematic reviews?
2. How (i) relevant (ii) useful and (iii) acceptable are these?

6.1.4 Search Strategy

Existing key systematic reviews (6-14) will be included, and repositories of relevant systematic reviews (Cochrane Database of Systematic Reviews; JBI Evidence Synthesis; NIHR HSDR & HTA Publications; NICE; PROSPERO Register) and electronic databases Medline, PsycLIT and CINAHL will be searched

from 2012 onwards using search terms derived from existing reviews (6-14) and search filters such as "systematic" and "meta-analysis". Reference lists of all included reviews, and the contents lists for the BMC journal Systematic Reviews will be hand searched. Included systematic reviews will then be 'mined' for primary studies.

6.1.5 Review Strategy

Two independent reviewers will screen titles and abstracts, and then full text articles, against the inclusion criteria using a piloted form in Covidence software. Disagreements will be resolved by consensus with reference to a third reviewer or the study Advisory Group as needed.

Inclusion criteria for reviews
Participants/ interventions: women who have undergone surgery for POP, SUI or mesh complications.

- Outcomes: any patient-related post-surgical outcomes, including pain, physical, functional, quality of life and psychological outcomes.
- Types of studies: systematic reviews.

Inclusion criteria for studies

- Participants: women who have undergone surgery for POP, SUI or mesh complications.
- Interventions: Instruments or items (PROMs, and PREMs) used to measure or record post - surgical outcomes from surgery for POP, SUI or mesh complications.
- Construct: patient related post-surgical outcomes, including pain, physical, functional, quality of life and psychological outcomes.
- Outcomes: psychometric properties of the measurement instruments: reliability and validity measures, and measures of engagement or responsiveness.
- Types of studies: primary quantitative studies included in systematic reviews; we will prioritise studies that focus on the development and/ or validation of measurement instruments.

Data extraction
Data will be extracted into categories mentioned above, mode of administration and setting/ context, and acceptability, onto a piloted form, by one reviewer and checked by a second reviewer.

Validity assessment and data synthesis
Psychometric properties may be assessed using established criteria (see above) and their validity assessed using COSMIN.[24] Results will be presented in a narrative synthesis which takes into consideration the validity, consistency of results and homogeneity of the studies. Any gaps against the PPI panel recommendations will be identified, as well as any examples of good instruments. Findings will inform the content of the new PROM and the next stages (1b and 1c) of the work package.

6.1.6 Patient and Public Involvement (PPI)

People with lived experience, from the PPI panel, will be involved in the planning, delivery and dissemination stages of both reviews, following Cochrane guidance.[25] They will help to identify and prioritise important items, domains, recall periods and response options, and advise on issues such as readability, cross-cultural applicability and appropriateness, likelihood to cause offence or distress.

6.2 Systematic Review (1b): A Qualitative Evidence Synthesis & Incorporating Findings Generated in the PURSUE Study (NIHR 202450)

6.2.1 Aim

To understand women's self-reported QoL impacts and experiences following surgical intervention for POP, SUI and mesh complications.

6.2.2 Method

Systematic review of qualitative studies, using qualitative evidence synthesis.

6.2.3 Review Questions

1. What are women's experiences in relation to their quality of life following surgical intervention for POP, SUI and mesh complications?
2. Do these vary/ are there any adverse QoL issues that are specific to some population groups at risk of health inequalities (e.g., black and minority ethnic women)?

6.2.4 Search Strategy

Medline, PsycLIT and CINAHL will be searched using search terms derived from existing reviews (6-14), with search filters or key terms such as "qualitative" and "interviews" applied.[27] Reference lists of included studies will be searched. If important evidence gaps are identified (e.g., experiences of black and minority ethnic women) we will also search for grey literature, using targeted Google searches and websites of relevant organisations.

6.2.5 Review Strategy

Two independent reviewers will screen titles and abstracts, and then full text articles, against inclusion criteria in Covidence software. Disagreements will be resolved by consensus with reference to a third reviewer or the study Advisory Group as needed.

McNiven and Toye, joint PIs on the PURSUE study (NIHR202450)[26], who have agreed to support this research, anticipate publishing the PROMs-related findings from their study in the next few months. This will be one essential output to include in this qualitative evidence synthesis. If their paper has not yet been published, they have kindly agreed to share their unpublished output with us.

Inclusion criteria

- Participants/ interventions: as per review 1a.
- Outcomes: as per review 1a.
- Types of studies: qualitative studies of any design, including qualitative components of mixed method studies.

Data extraction

Data will be extracted into categories mentioned above by one reviewer and checked by a second reviewer.

Validity assessment

Validity assessment will be carried out by one reviewer and checked by a second, using an adapted version of the CASP checklist for qualitative studies.[28]

Data synthesis
A framework synthesis approach will be used to triangulate concepts with the findings from review 1.[29-30] If gaps have been identified in review 1, thematic synthesis[31] or meta-ethnography (if data are sufficiently rich) may also be used.[32] The review will be reported following updated PRISMA guidance.[33]

6.2.6 Patient and Public Involvement (PPI)

As per the systematic review of reviews (1a).

6.3 Outcome from Studies 1a & 1b

Outcome from studies 1a and 1b: the production of a preliminary conceptual framework of the domains and items that may need to be included in the PROM. This preliminary conceptual framework will inform the semi-structured interview schedule to be used in study 1c described next.

6.4 Secondary Data Analysis (1c): Incorporating the Findings of the PURSUE Study (NIHR 202450)

6.4.1 Aim

To understand the impact and experience of surgery for POP, SUI or mesh complications on quality of life from the patient's perspective using a highly relevant subset of the PURSUE study data.

6.4.2 Methods

A secondary data analysis of a highly relevant subset of data generated in the PURSUE study (NIHR 202450). From their participant sample of 74 women, 25 (34%) had either SUI and/or POP and have had/or are waiting for urogynaecology surgery. In particular, this sample includes:

- Women with SUI and have had urogynaecology surgery = n.19
- Women with POP and have had urogynaecology surgery = n.15
- Women who have had mesh for POP and/or UI = n.18
- Women who report mesh-injury complications = n.16
- Women who have had mesh revision or removal surgery = n.7
- Women waiting for/in discussions about mesh revision or removal surgery = n.6

A secondary data analysis of this data is required to ensure that all information that could be relevant to the development of the PROM has been identified from this dataset, as some may have been omitted in the PURSUE team's broader approach to the analyses of their data and subsequent presentation of their findings in their manuscripts

6.4.3 Data Collection

Our research associate at LBU will undertake the secondary data analysis (supported by the research associate at the UoS if needed). The PURSUE study team will share the final, approved versions of the

25 interview transcripts for the secondary data analysis (checked to ensure they are deidentified and any details participants wished to be redacted had been removed), along with supporting tables on socio-demographics.

6.4.4 Data Analysis

A framework approach to data analysis will be undertaken. This will be shaped by *a priori* categories related to findings from the relevant literature (including the findings from NIHR 202450 generally), requirements of the NIHR (e.g. patient experience), along with an inductive analysis of a sample of our transcripts. From the themes identified, items will then be drafted to reflect this content. Language used in the transcripts will be drawn upon to generate the PROMs initial items in the first instance for consideration in WP2 by the whole study team, PPI panel, advisory and other stakeholder groups as per 1d described below.

6.5 Gathering Further Direct Patient Input via Qualitative Interviews (1d)

6.5.1 Aim

To understand the impact of surgery for POP, SUI or mesh complications on quality of life from the patient's perspective.

6.5.2 Methods

A qualitative study design using an overarching phenomenological theoretical framework will enable us to understand the phenomenon of interest through the lens of the participant, thus ensuring high content validity.[34] Concept elicitation interviews will be conducted. Whilst the overall PURSUE study findings are very relevant to our work, and the surgical sample of 25 (described in study 1c above) is highly relevant, we will also need to include women who have undergone other certain surgical procedures, women whose surgery was many years ago or more recent, and those with disability as the PURSUE study sample lacks these (please see study 1c). Women from more diverse ethnic backgrounds is also a priority as the PURSUE team have confirmed that ethnicity (self-identified) is White British (n.20); white Scottish (n.2); white Welsh (n.1); white Irish (n.1); and Afghan sikh (n.1) in their surgical sample of n=25, and furthermore only 10/74 of their interviews were from minority ethnic groups. We also need to explore women's views of preferred response options, format, mode of administration and barriers and facilitators to completion of a PROM which was outside of the scope of their study. Our further concept elicitation interviews will address the gaps in the PURSUE study sample and address PROM-specific issues that were beyond the scope of that study.

6.5.3 Sample and Sample Size

We intend to undertake semi-structured interviews and explore PROM related issues as well as women's QoL post-surgery with a further 30 women. Qualitative interviews with up to 30 women should be sufficient, but we will also continue to interview women in our study until information power has been achieved, so it is possible that the final sample size may exceed 30. Of note is that chief investigator GLJ is a co-applicant on NIHR 201492 to develop a PROM to measure gastro-intestinal recovery and 29 qualitative interviews have recently proved sufficient to reach information power in this study too. We will undertake purposive sampling by the three surgical groups (approx. 10 from each of the three groups) and aim for maximum diversity ensuring representation from

women with different socio-demographic characteristics (such as age, ethnicity and socio-economic background), type of surgery and outcome (positive or negative), and outcomes at different times post-surgery (short and long-term).

6.5.4 Data Collection

Our research associate will undertake the 30 interviews. A semi-structured interview topic guide will be used, designed to ask specifically about QoL impacts following surgery, and then to explore PROM-related issues. This topic guide will be informed by the NIHR 202450 publication, and discussions with them with recourse to their data, and other relevant themes identified from the systematic reviews. Interviews will last between 60-90 minutes. They will be audio recorded and transcribed verbatim. They will be undertaken face-to-face, by telephone or virtually depending on interviewees' preferences. Some women may prefer to undertake the interview in a language other than English and we have requested funding for interpreters to assist with these interviews

6.5.5 Data Analysis

AOC, GLJ, and the Research Associate will analyse the data from the 30 interviews. We will use 'framework' analysis to understand the ways in which surgical treatment for POP, SUI and MESH complications have impacted upon QoL and to combine the findings from 1a to 1c.[35] In particular, early findings from the preliminary conceptual framework generated from the systematic reviews (including the findings from NIHR 202450) will help shape the thematic framework used in this analysis, along with inductive analysis of a sample of our transcripts. The thematic framework will also be shaped by *a priori* categories related to PROM format: preferred response options, mode of administration, and barriers and facilitators to completion as part of clinical effectiveness studies. From the themes identified, items will then be drafted to reflect this content. Language used in the transcripts will be drawn upon to generate the PROMs initial items in the first instance for consideration in WP2 by the whole study team, PPI panel, advisory and other stakeholder groups. Given the need for the PROM to be available electronically, items will be presented on paper and on an electronic platform (Qualtrics). We will ensure that any differences between the paper and electronic version are non-substantive or minor so that further equivalence testing is not required in the future based on best practice guidance.[36] There will be no change in content or meaning and changes will only be non-substantive (e.g. either circling a response or clicking the response on a screen), or minor (e.g. either having multiple items on a page, or one item per screen).[36]

6.5.6 Patient and Public Involvement (PPI)

PPI members will help to refine ways of approaching women, comment on patient-facing documentation such as the invitation letter to ensure these documents are engaging and acceptable, read a small number of anonymised transcripts before discussing preliminary findings, and shape the report of findings to be presented to WP2 participants.

6.6 Outcome from Work Package 1

A prototype questionnaire (paper and electronic formats) with an initial long pool of items and domains underpinned by a conceptual framework that was informed from systematic reviews of the literature, findings from NIHR 202450, including a secondary data analysis, and further concept elicitation interviews. Next will be to gather stakeholder feedback on these initial items and domains, assess user acceptability of the PROM, ensure that there are only minor modifications between the

modes of administration and the item pool can be easily translated and has cross-cultural applicability. This work will be carried out in WP2 described below.

7. WP2 (Months 12-18)

To confirm the face validity, minor modifications between the modes of administration and translation of the PROM, we will gather stakeholder feedback (2a), assess user acceptability (2b), and undertake a translatability assessment to ensure the PROM is acceptable to users and has cross-cultural applicability (2c).

7.1 Gathering Stakeholder Feedback on the PROM (2a)

7.1.1 Aim

To gather stakeholder feedback on the item pool and paper and electronic format of the prototype version of the PROM.

7.1.2 Method

Full-day, face to face workshop with the study team, our PPI panel and an expert advisory group. The advisory group will comprise a representative from NHS digital, and our collaborators including AM and FT from NIHR 202450, Dr Fiona Reid (Chief Investigator on NIHR 133665 the Follow up PROSPECT Study) and JEB, University of Sheffield. If successful, we will also immediately invite other key stakeholders to join the advisory group, including Baroness Cumberledge (who we will invite to independently Chair this group), a representative from NICE, Dr David Churchman, Founder and Managing Director at Inspired Health Outcomes Limited (IHO). They will be invited to review the content of the PROM and confirm that the differences between the paper and electronic versions are only at most minor, without any chance in content or meaning between the two versions.[36] Perceived implementation barriers to PROM use in clinical effectiveness studies, and opportunities for academic, clinical and public dissemination opportunities will also be discussed. The PPI panel will be asked if they would prefer/like to have a pre-meeting before the one-day meeting which has worked well in other PROM development studies undertaken by members of this team.

7.1.3 Sample Size

This will include the study team, the PPI panel and advisory group members.

7.1.4 Data Collection

We will adopt a similar approach to data collection as that used in the development of PROMs by members of our study team. All items will be placed on post-it notes in the room and people will be invited to vote for each item, and/or add new items if anything is considered missing. This feedback will then be collated and discussed later during the meeting. The meeting will be recorded to ensure all points are taken into consideration, but the main approach will be the study team listening to stakeholders and acting on their contributions to facilitate the feasibility, acceptability, and validity of the PROM.

7.1.5 Data Analysis

Pragmatic notetaking and count data. The recorded session will also be transcribed and reviewed to ensure all relevant information has been captured from the meeting. Following any modifications, the user acceptability of the PROM will then be assessed in WP2b described next.

7.2 Assessing the User Acceptability of the PROM (2b)

7.2.1 Aim

To assess the user acceptability of the prototype versions (paper and electronic) of the PROM with patients.

7.2.2 Method

Qualitative cognitive debriefing interviews, which is considered standard practice in the development of a high-quality PROM.[37-38] The information obtained from the interviews can be used to infer the participants cognitive thought process as they comprehend the question, recall information, and select a response.[37,39] Cognitive interviewing also provides assurance of the measure's content validity (the extent to which the content of the PROM adequately reflects the construct being measured) and is a useful method for refining the draft instrument based on the participants responses[34], and will ensure the acceptability and equivalence of the electronic version.

7.2.3 Sample Size

The interviews will be undertaken with 30 patients including 10 women who have undergone surgery for POP, 10 who have undergone surgery for SUI and 10 who have had surgery because of mesh complications, which should be sufficient for developing questionnaires.[39]

7.2.4 Data Collection

The interviews will start with the think-aloud process whereby participants will be asked to verbalise their thoughts whilst completing either the PROM on paper or electronically (15 in each group). Any key observations or difficulties will be recorded i.e., reading difficulty, pauses, skipping questions. The participants will then be asked a series of questions (from a standardised topic guide) for each item to solicit their views (relating to item interpretation, the response categories and time frame). The cognitive interviews will document the content validity, clarity and comprehensibility of the PROM, as recommended by the (FDA). A definition list will also be created prior to conducting the cognitive interviews so that the interviewer can determine whether the participants understand the items as intended.[40] The interviews will be audio-recorded, and the researcher will note down any key observations during the debriefing exercise.

7.2.5 Data Analysis

Following the interviews, the expert steering group and PPI panel will be invited to review the participants' comments and help make any modifications to the instrument. The study will use an 'item tracking matrix', recommended by the FDA[3] to document any changes to the items and reasons for those changes.

7.2.6 Patient and Public Involvement (PPI)

PPI members will be involved in the planning, and delivery of the cognitive interviews. They will help to develop the standardised topic guide and advise on issues that may impact upon the think-aloud exercise such as appropriateness, likelihood to cause offence or distress. They will also read a small number of anonymised transcripts before discussing preliminary findings, to shape the version of the PROM that is sent for translatability assessment described next.

7.3 Translatability Assessment (TA) of the PROM (2c)

7.3.1 Aims

To ensure the PROM has cross-cultural applicability and can be easily translated into other languages and cultures for application in the UK and in other territories.

7.3.1 Methods

This will follow best practice guidelines for PROM translation[41] and be undertaken under the direction of Professor Jenkinson with Dr David Churchman.

7.3.3 Data Collection

The first step of the TA is a thorough review of the new instrument by a highly experienced PROM translation and linguistic validation expert, selected by Dr David Churchman. This expert will initially review and provide feedback on the new PROM in terms of ease of completion and general use. The same Translation and linguistic validation expert will then develop a Concept Elaboration Document (CED). This will be produced to provide potential translators further clarification of the underlying concepts being assessed by questions in the measure should a simple direct translation of the source material not be possible/meaningful in a target language. The translatability of the questionnaire will then be assessed across a variety of languages (to be determined by the research team in consultation with IHO). The process will involve 'in-country' translators assessing the ease with which the original English language version of the measure can be translated into the target foreign languages.

7.3.4 Data Analysis

Each reviewer will be asked to provide recommendations on the suitability of the original text for translation and, in instances where translation may prove challenging, is invited to suggest modifications to the original text to improve ease of translation. Recommendations from all translators will be fed back to the project team who will consider recommendations and make alterations to the original text accordingly during a project team meeting. We will invite a subset (n=12) of our original interviewees in the UK from exercise 2b to take part in a second round of cognitive debriefing interviews to comment on the resulting questionnaire suggested from the translatability assessment to confirm that any adjustments made are acceptable and meaningful to patients. New patients may also need to be recruited though depending on the response rate for this activity.

7.4 Outcomes from Work Package 2

The outcomes will be a concept elaboration document and a prototype long-form PROM with an initial pool of items and domains that has been reviewed by stakeholders and patients, checked for minor modifications between the modes of administration, has face validity and is easily translatable. The next stage will be to evaluate the psychometric properties of the initial item pool which will be undertaken in WP3.

8. WP3 (Months 19-34)

To establish the PROMs psychometric properties we will undertake one survey to reduce its item number and identify its domain structure (3a) and a second survey with a new sample of women to confirm its domain structure, reliability, validity, and responsiveness in the context of short-term surgical outcomes (3b).

8.1 Survey (3a): To Reduce the Number of Items and Identify the Domains and Scoring Algorithms of the PROM (Months 19-22)

8.1.1 Aim

To reduce the number of items and identify the domains and scoring algorithms of the PROM

8.1.2 Method

Postal/online survey based upon patient preferences.

8.1.3 Sample and Sample Size

We will survey women from our target groups who have undergone surgery for POP, SUI and mesh complications in the past. Patient identification will take place before month 19. We aim to include 250 women in our analysis, based upon exceeding the minimum responses needed for exploratory factor analysis (100+ women).[42] Statistical adequacy of sample size will be verified based on the KMO Test, Bartlett's Test of Sphericity and an analysis of the communalities and the number of items per factor.[43] More data will be collected following best practice if there are a larger number of items in the PROM, and the thresholds are not met according to our sample size indicators. In anticipation of a response rate of around 70%, surveys will be sent to 350 women.

8.1.4 Data Collection

Women will be invited to complete a paper or electronic versions based on their preferences.

8.1.5 Data Analysis

Levels of missing data and item responses will be presented back to the team and PPI panel to consider the findings and ascertain if the item/s are sufficiently important to include in the exploratory factor analysis. Exploratory factor analytic techniques, along with other standard psychometric tests to identify items and domains will then be undertaken. The factor analytic technique and rotation method will be decided upon based upon our assumptions about the correlations between the scales following our work in WP1. To extract the factors, corresponding eigenvalues greater than 1, scree plots and minimum factor loadings of 0.60 are likely to be selected. Descriptive statistics at domain level (including missing data, means, maximum endorsement frequencies, floor and ceiling effects

amongst others) will be explored. Internal consistency reliability, inter-item and item-total correlations will also be calculated. Given that there will be only non-substantive/minor modifications between the paper and electronic version, no equivalence testing is needed and all responses will be analysed in one data set.[36]

8.1.6 Patient and Public Involvement (PPI)

PPI members will help to refine ways of approaching women, and comment on patient-facing documentation. They will also help shape the final version of the PROM. The results of the missing data analysis (missing items, floor/ceiling effects, etc) and psychometric testing will be presented back to the team and PPI panel to consider if the items are sufficiently important to include in the EFA and final measure before being used in survey 3b.

8.2 Outcomes from Work Package 3a

A shorter version of the PROM, with the domain structure, scoring algorithms and final item pool established. i. This final version of the PROM needs further psychometric testing for reliability, validity, responsiveness and minimally important differences which will be undertaken in WP3b in the context of short-term surgical outcomes and WP4 in the context of longer-term surgical outcomes. ii. The data associated with these final items in the PROM, will also be used to derive the health classification system for the preference-based measure in WP5.

8.3 Survey (3b): To Confirm the Psychometric Properties of the Final Version of the PROM in the Context of Short-Term Surgical Outcomes in a New Data Set

8.3.1 Aim

To confirm the domain structure, reliability, validity, responsiveness and minimally important differences of the PROM in the context of short-term surgical outcomes up to 6 months post-surgery.

8.3.2 Method

Postal/online survey based upon patient preferences.

8.3.3 Sample and Sample Size

To achieve a minimum new sample of **300** women required for our confirmatory factor analysis (CFA)[44], and in anticipation of a response rate of around 70%, we will administer our survey to at least 430 women. Based on the frequency of the different interventions in the NHS (see page 4), the sample will include:

- **150 (215 approached)** women having surgery for POP. Currently, mesh is only used in abdominal procedures. This means we expect to recruit 10 women who are having abdominal mesh and 140 women having alternative surgery.
- **100 (143 approached)** women having surgery for SUI, none of which will be with mesh, because this procedure is not currently being conducted.
- **50 (72 approached)** women having mesh complication surgery.

We will undertake an analysis of the communalities and the number of items per factor to confirm the adequacy of the sample size as per Survey 3a.[43] These sample sizes are also adequate to meet the thresholds for the responsiveness and minimally important difference analysis reported below.[45]

8.3.4 Data Collection

Women will complete the PROM before surgery, and then at 3 months and 6 months post-surgery, along with other selected instruments identified in WP1. To assess test-retest reliability, a subsample of women in each group will be asked to complete the PROM at two time points one week apart before surgery. To establish test-retest reliability women will complete the PROM twice, one week apart. The exact time is to be confirmed but is anticipated a week after the completion of the 3-month post-surgery PROM when patients are more likely to be stable and there is time in the study to collect this data rather than 1 week post 6-month completion.

8.3.5 Psychometric Analysis

We will undertake a number of psychometric analyses consistent with best practice for developing robust PROMs.[3-6] The tests will include assessing levels of missing data and response patterns, CFA, internal consistency reliability, test-retest reliability and construct validity including known groups validity and convergent validity. It has been reported that scale validity is supported if at least two different forms of construct validity have been assessed.[46] Known groups validity will be examined by testing *a priori* hypotheses pertaining to comparisons of the PROM scores between subgroups of patients defined by their surgical, demographic and other clinical characteristics (e.g., POP, or SUI). Convergent validity will be assessed by comparing the results of our PROM with other similar measures (selected following our work in WP1). To assess the PROMs responsiveness, four different statistical distribution-based methods will be used including: i. effect size, ii. standardised response means, iii. significance of change, and the iv. responsiveness statistic comparing the findings across all three time points. Minimally important differences will be calculated using an anchor-based method along with *a priori* hypotheses and receiver operating characteristic (ROC) curves to identify important changes in the new PROM that discriminate between participants who self-report as having improved vs. not-improved as recommended by the COSMIN guidelines.[5,47] Finally, we will use a MIMIC model to check that there is no construct bias in the PROM.

8.3.5 Patient and Public Involvement (PPI)

The PPI panel will help to refine ways of approaching women, and comment on patient-facing documentation. The results of the missing data analysis (missing items, floor/ceiling effects, etc) and CFA analysis will be presented back to the team and PPI panel to consider, should changes to the item pool and domain structure be required.

8.4 Outcomes from WP3

A fully validated PROM with its domain structure, reliability, validity responsiveness and minimally important differences psychometrically established in the context of short-term surgical outcomes up to 6 months post treatment.

9. WP4 (Months 23-34)

To next confirm the psychometric properties of the PROM in the context of longer-term surgical outcomes we will undertake a survey with women at least 6 months post-surgery (4a) and another survey of long-term surgical outcomes in the context of a clinical trial (4b).

9.1 Survey (4a): Establishing the Psychometrics of the PROM in the Context of Longer-Term Surgical Outcomes in a New Dataset

9.1.1 Aims

To confirm the domain structure, reliability, and validity of the PROM in the context of longer-term surgical outcomes (6 months onwards).

9.1.2 Method

Postal/online survey based upon patient preferences

9.1.3 Sample and Sample Size

To achieve a new sample of **300** women who are between 6 months and 14 years post-surgery, based on the statistical requirements of CFA and in anticipation of a response rate of around 70%, we will administer our survey to at least 430 women. We will undertake an analysis of the communalities and the number of items per factor to confirm the adequacy of the sample size as per Survey 3a and 3b. Based on the frequency of the different interventions in the NHS (see page 4), the sample will include:

- **150 (215 approached)** women who have undergone surgery for POP (75 with mesh and 75 without).
- **100 (143 approached)** women who have undergone surgery for SUI (50 with mesh and 50 without).
- **50 (72 approached)** women who have had mesh complication surgery.

9.1.4 Data Collection

Women will be invited to complete the PROM and then to assess test-retest reliability, again one week afterwards.

9.1.5 Data Analysis

As described in WP3b. However, the responsiveness and minimally important difference tests which will not be assessed because it will not be possible to administer our PROM before surgery in this cohort of women.

9.1.6 Patient and Public Involvement (PPI)

The PPI panel will help to refine ways of approaching women, and comment on patient-facing documentation. The results of the missing data analysis (missing items, floor/ceiling effects, etc) and CFA analysis will be presented back to the team and PPI panel to consider, should changes to the item pool and domain structure be required.

9.2 Survey (4b): Establishing the Psychometrics of the PROM in the Context of a Clinical Trial in a New Dataset

9.2.1 Aim

To confirm the domain structure, reliability, and validity of the PROM in the context of a clinical trial.

9.2.2 Method

Survey to women in the PROSPECT Follow-up trial who underwent POP surgery (with or without mesh).

9.2.3 Sample Size

The survey will be distributed to a new sample of approximately **400** women between 12 and 14 years post-surgical intervention.

9.2.4 Recruitment (Months 23-28)

Women will be recruited from across the whole Prospect cohort follow-up study. Based upon correspondence with the Prospect team, approximately 80 women per month return their follow-up questionnaires, meaning we anticipate receiving approximately 400 questionnaires during the recruitment window.

9.2.5 Data Collection

The PROSPECT Team is following up women every two years. By 2025 (which is when we would be planning on undertaking WP4b, every woman in their study will be between 12-14 years post-surgery. The Prospect team will administer our PROM along with the POP SS (their primary outcome measure), and others included in their study (e.g., the EQ-5D). This team will enter the data and send us an anonymised data set including the responses of these outcome measures. Currently, no ethnicity data is collected on this trial. Therefore, we will also include an ethnicity proforma with our PROM and questions about how they have found completing our measure as part of this clinical trial.

9.2.6 Data Analysis

Domain responses, CFA, reliability (internal consistency and test-retest), construct validity (known groups and convergent). Data will also be compared across the different intervention groups. Finally, we will use a MIMIC model to check that there is no construct bias in the PROM.

9.2.7 Patient and Public Involvement (PPI)

PPI members will help to refine ways of approaching women, and comment on patient-facing documentation. The results of the missing data analysis (missing items, floor/ceiling effects, etc) and CFA analysis will be presented back to the team and PPI panel to consider, should changes to the item pool and domain structure be required.

9.3 Outcome from Work Package 4

A PROM with its domain structure, reliability, validity and responsiveness psychometrically established in the context of longer-term surgical outcomes, and a clinical trial. Running concurrently with WP3b and WP4 will be the development of a preference-based version of the tool for use in economic evaluations which is described below:

10.WP5 (Months 23-34)

Aim: To generate a preference-based measure (PBM) from the PROM developed in WP3a to calculate QALYs for use in economic evaluation of interventions. Preference weights can be applied to prospective and retrospective PROM datasets.

Methods: The derivation of the preference weights will follow a well-documented process made up of 5 steps[48] using discrete choice experiments (DCE).[49] NICE recommends that utilities should be based on preference of the general population for use in health technology assessment.[50] In this research, POP, SUI and mesh complications affect only women and it is anticipated that differences in public and patient preferences may be of significance, meaning the research would benefit from comparisons of each to understand any differences, and for many applications the preference weights from patient preferences could be more relevant.

10.1 Step 1: Development of the Classification System for the APPRAISE PBM

For the classification system, we will select 8 and 10 items from the shorter version of the PROM at the end of Stage 3a. We will first consider the dimensionality of the APPRAISE measure using confirmatory analysis to inform the next set of analyses. Rasch analysis will be used to exclude any misfitting items and select the items with the best psychometric properties. This method was originally developed in the estimation of a preference-based measure of health from the SF-36[51-52] and subsequently used by the ScHARR team to generate a large number of condition-specific preference-based measures including urinary incontinence[53], overactive bladder[54], cancer[55], dementia[56] and mental health[57] among others. The items selected will be discussed with the PPI panel to ensure face validity with the APPRAISE PROM.

10.2 Step 2: Selecting Profiles for DCE Survey

The DCE tasks ask respondents to choose between 2 profiles: health description A and health description B, where each profile is made up of a selection of one level for each item in the classification system. To enable the values to be used to generate QALYs, the preference weights will need to be anchored onto the usual 1--0 scale where 1 and 0 represent full health and dead respectively. This will be achieved by including an additional attribute for duration in the DCE (often called DCE_{TTO}).[58] Duration levels will be informed by the literature with input from clinicians and PPI. As it will be infeasible for participants to value all possible combinations of health states, we will select a subset of profiles via D-optimal methods[59] to produce a design able to estimate a pre-specified regression model optimised for the multinomial logit model which is the most common model estimated for such DCEs.[60]

10.3 Step 3: Pre-Piloting DCE Survey

Once the profiles have been generated, the PPI panel will be asked to co-produce the wording of instructions, preambles and display of the tasks. We will also interview up to 10 participants recruited from a convenience sample to test whether the tasks are being understood as intended.

10.4 Step 4: Pilot Survey

The pilot survey will include 50 participants from the general population and 50 from women with pelvic floor problems to ascertain that the participants are able to complete the tasks with data recorded as intended.

10.5 Step 5: Main Valuation Surveys

10.5.1 Sample Size

1000 individuals from the public representative of the UK population for age and gender and 600 women with pelvic floor disorders screened from the public will be recruited. There is no consensus on sample size, but previous research has found the proposed sample to be sufficient.[49]

10.5.2 Recruitment

Participants will be recruited by a market research agency via existing online panels. Women with pelvic floor problems will be approached through existing panels and screened from public panels. The agency we have worked with previously has confirmed the samples requested are feasible.

10.5.3 Data Collection

After consenting to the survey, participants will complete sociodemographic and health questions. All participants will view information describing what it is like to live with pelvic floor post-surgery complications and complete the APPRAISE classification to familiarise themselves with the health state wording in the DCE tasks. Third, participants will complete one practice question followed by 8-12 DCE tasks.

10.5.4 Data Analysis

DCE data will be analysed separately for public and patients using a multinomial logit model with cluster-adjusted standard errors, modelling the choice using dependent variables of the severity levels of each item interacted with duration, plus duration.[58] Anchored values are generated by dividing each coefficient by the duration coefficient. In the final model and preference weights per population (public/patient), more severe health and complications will lead to lower utility values. Once the utilities are produced, we would use the data from Stage 4b to compare the psychometric properties of EQ-5D with the new PROM.

10.6 Outcome from Work Package 5

A preference-based version of the PROM with weights elicited from the public and patients. It will be possible to apply the weights to datasets with APPRAISE data to compute QALYs for use in evaluating interventions for women with POP, SUI and mesh complications. These algorithms will be made freely available for public funded use and research. A psychometric comparison between the EQ-5D and the new PBM.

11.WP6 (Months 6-34)

11.1 To Assess Implementation Barriers to PROM Use in Clinical Effectiveness Studies

11.1.1. Aim

The aim is to explore facilitators and barriers to implementation of the PROM within clinical effectiveness studies.

11.1.2 Methods

We will do this by identifying barriers and mitigation strategies across the whole six WPs including the qualitative interviews with women in WP1 and with stakeholders in WP2 (WP6a); and assessing completion rates, including for different socio-economic and ethnic groups as part of WP3 and WP4 (WP6b).

11.1.3 Sample

In addition to the work cited above, we will also interview 18-20 hospital staff from 6 UK BSUG recruitment sites, and 8-10 trialists to identify potential implementation barriers and solutions (WP6c). A purposive sample of hospital staff involved in collecting or using the PROM will be used (clinicians, hospital managers and administrative staff). We are well placed to do this because our clinical team members lead RCTs or recruit for such RCTs and we are collaborating with the PROSPECT study team in this study.

11.1.4 Data Collection

Interviews will take place face-to-face, by telephone, or virtually dependent on interviewees' preferences. During the interviews we will present the PROM and a draft user manual. This user manual will be based on the WP1 patient interviews, WP2 stakeholder feedback, and the evidence base on implementing PROMs generally[61-63], in clinical trials[64] and relevant theoretical frameworks to improve implementation or change behaviour e.g., the Consolidated Framework for Implementation Research[65] and the Theoretical Domains Framework.[66] Interviews will last around 60 minutes, be recorded and transcribed verbatim.

11.1.5 Data Analysis

We will use framework analysis to identify any PROM specific implementation issues and develop an implementation strategy to mitigate these in different scenarios.

11.1.6 Patient and Public Involvement (PPI)

The women's views will be collected in WP1. We have described earlier how PPI members will be involved in recruitment, analysis and reporting of findings of women's views. PPI members will be involved in the staff interviews in the same way.

11.2 Outcomes from Work Package 6

Qualitative evidence to identify what may inhibit or facilitate use of the PROM in clinical effectiveness studies. The production of a user manual to address these issues and facilitate its utility.

12.Final Stage of the Research (Months 35-36)

In the final two months, we will focus upon completing our dissemination activities, writing up the final report and remaining publications, data archiving and storage.

12.1 Research Outputs

We will produce:

- The APPRAISE PROM to be made freely available for publicly funded use and research in clinical effectiveness studies, in both paper and electronic formats.
- A preference-based version of the PROM for use in economic evaluations.
- A published study protocol.
- A concept elaboration document to support ease of translation of the PROM into different languages.
- A dedicated project website hosted at Leeds Beckett University.
- Infographics for circulation across social media – targeted at patients and healthcare professionals.
- A YouTube video to provide a layperson's summary of the project findings.
- Publications from each of the six work packages in high-impact open access journals, and clinical practice guidelines (e.g., RCOG, NICE).
- Conference presentations for national and international academic, clinical and patient audiences.
- A user manual to facilitate the use of the APPRAISE PROM to enable all women to self-report the impact of pelvic floor surgery upon their QoL.
- Open access data arising from the individual work packages planned in this programme of work.

12.2 Dissemination

To actively engage and communicate with the end-users of our PROM, we will co-develop and psychometrically test the PROM in partnership with our PPI co-applicant and PPI panel to ensure it is patient-centred and meets their needs. We will disseminate the outcomes of each work package to patients and healthcare professionals as they are completed using plain English language targeted outputs for each of these audiences. These will include infographics and newsletters that will be circulated via a dedicated project Twitter account, professional societies (e.g. BSUG) and dedicated research project webpage. We will engage with third sector organisations e.g., Health Talk (www.healthtalk.org) who have already agreed to include links to our PROM on their website. We will produce a YouTube video using subtitles and audio description to explain how we developed the PROM, how patients co-developed this with us, what it is used for and how it works - content all informed by PPI. We will present at patient focused, clinical and academic conferences to disseminate our work such as the International Urogynaecology Association Annual conference, the BSUG national conference, ISOQOL and the national PROMs conference. We will liaise with our institutional press office, and those more widely e.g., at NHS England, NICE and NHS digital to create news stories for their websites, and we will disseminate the study at key milestones via the mainstream media.

12.3 Ensuring the Adoption of the PROM into Healthcare

Our PROM will be made freely available for public use (and publicly funded research) removing any financial barriers to utility. A Community of Practice (CoP) will be established. This will be led by joint

lead SJ who, once the study is completed will be the APPRAISE PROM Champion. She will work with the clinicians associated with this project to adopt the measure and promote its use with colleagues in other hospital trusts and private clinics. We will produce a freely available user manual to support use by healthcare professionals, accessible via the project webpage and also circulated via our established clinical networks. We will also continue to build partnerships during the project with trialists and other relevant urogynaecological units that would be a potential end user of our tool, so that over time, our CoP will help to share best practices amongst Trusts on using and integrating this PROM into clinical effectiveness studies. To further ensure adoption into clinical practice, NHS Digital have already agreed to field test the final PROM electronically to ensure linkage with The Surgical Device and Implant Registry and independent submission of the PROM by patients. We will have demonstrated the acceptability of the electronic version of the PROM, ensuring that migration will be easily achieved without the requirements to undertake further equivalence testing. Our current relationship with NHS digital means that we are already working closely together both in an advisory capacity and as a key centre in the mesh removal service. Dr David Churchman via IHO has a proven track record of promoting PROMs via the IHO dedicated website and at academic and industry conferences. Our team members also have existing relationships with NHS England via the Policy Research Unit at ScHARR, University of Sheffield and NICE via the Sheffield Decision Support Unit, also based at ScHARR to facilitate use of the PROM.

12.4 Anticipated Impact

In the short-term we will have a major impact upon on women requiring surgery for these conditions and all other key stakeholders involved in the surgical management of women living with POP, SUI and mesh complications by producing, in plain English language, a psychometrically robust and freely available PROM (in paper and electronic formats) that can assess the short- and long-term outcomes and experiences of surgery for SUI, POP and mesh complications. Its preference-based version will also enable the calculation of QALYs in economic evaluation of interventions for women living with POP, SUI and mesh complications, thus supporting policymakers to determine the best treatment decisions. In the longer-term, our PROM will be adopted by NHS Digital and as a result of our translatability exercise and production of the concept elaboration document can be easily translated into other languages increasing the reach and impact of our tool.

13. Sharing the Progress and Findings of the Research with Study Participants

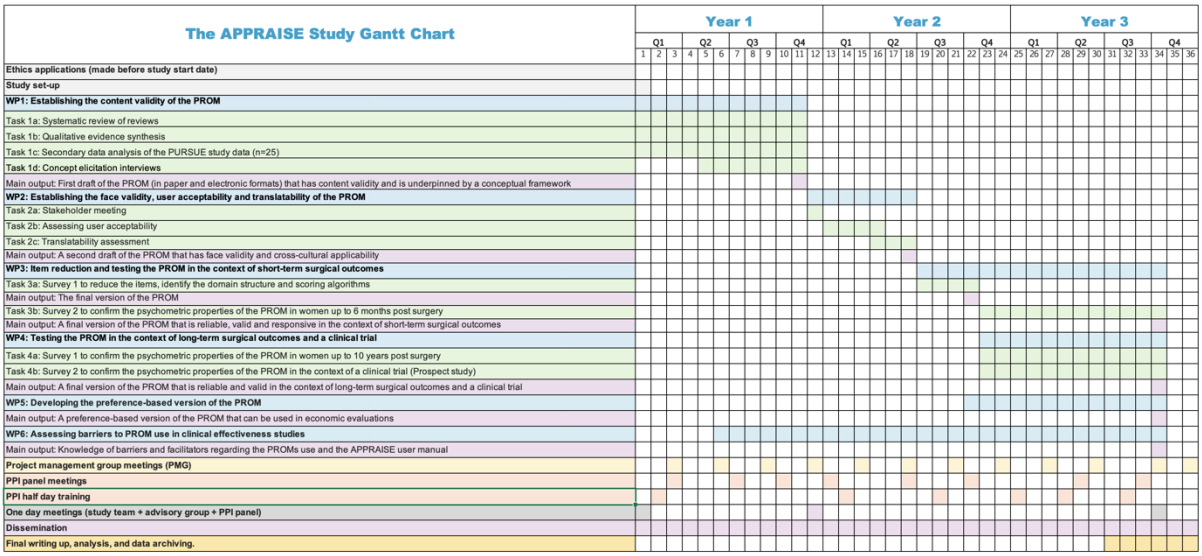
At the end of each WP (or individual study within the WP where relevant e.g., study 2b) we will send a lay summary of the findings, produced in collaboration with the PPI panel to all the study participants. We will also upload these to our project webpages. We will signpost patients to the plain English language summary in patient information sheets, and on all our other patient-facing material (e.g., debrief forms) and include the plain English summary in our final report. Different language versions and the paper and electronic formats will be created in consultation with the PPI panel at the start of the study.

14. Ethics

Ethics approval for this study will be sought from Leeds Beckett University, the University of Sheffield (WP5) and HRA for each WP where relevant. The study will also conform to the UK Framework for Health and Social Care Research and the BPS Human Research Ethics guidelines. All participants will be aged 16+. The main ethical issue is ensuring that informed consent to participate in this study is obtained. All patient-facing material will be written and produced in consultation with our PPI panel

to ensure that our Participant Information Sheet explains the purpose of the study, their role, and information on confidentiality, risks, and the consent process in an appropriate way. All participants will be given the opportunity to ask any questions and given a one-month time frame from the completion of the PROM or interview to withdraw their data. There is the potential for the study to increase anxiety and worry for the women about the outcomes of surgery for POP, SUI and mesh complications. Participants will be provided with a debrief document following their participation as recommended by the BPS, explaining the expected outcomes of the research and signposting to free support services, as well as reminding them how we will maintain their confidentiality, their rights for data withdrawal, and our processes for updating them about our findings.

15.Project/Research Timetable



16. Project/Research Expertise

Lead applicant Professor Jones (GLJ) is a health psychologist, chartered psychologist and full BPS member of the Division of Health Psychology and Psychology of Women and Equalities Section whose primary expertise is in developing and validating PROMs in women's health and for use in clinical effectiveness studies. For example, her Endometriosis Health Profile-30 is used as the primary outcome measure in several high profile NIHR funded clinical trials. She will manage the budget, oversee and contribute to all work packages, lead WP3 and WP4, supervise the full-time Grade 7 Senior Research Fellow, full-time project officer, research fellow (60%) and research assistant (40%) at LBU. CJ is a health services researcher whose expertise is in developing and validating PROMs and undertaking translatability assessments. He will lead WP2. DR and AK are health economists. Their expertise is in measuring and valuing health and deriving health state utility values from PROMs. AK will lead WP5, with guidance throughout from DR. AOC is a health services researcher with expertise in qualitative and mixed methods research. She will lead the qualitative work in WP1 and WP6 and supervise the part-time qualitative researcher at the University of Sheffield. SJ, SD, TG, and SR are all consultant urogynaecologists who work in NHSE commissioned POP/SUI centres, with strong research portfolios in the area of pelvic floor dysfunction and PROM development and use in clinical practice. SJ is joint lead, immediate past Chair of the BSUG and Clinical Lead for the Sheffield mesh complication centre, which SCR also works in. She will oversee all recruitment, and clinical content, the inclusivity

aspects of the research and be the clinical champion for the PROM. SD is part of I-Chorus.org, the team undertaking the development of COS in urogynaecology. SCR, TG and SD will lead on patient recruitment in Sheffield, Norfolk, Surrey and London respectively. StB is Past President of the Association of Coloproctologists. He has over 25 years clinical experience in pelvic floor surgery and will support patient recruitment and provide colorectal expertise throughout. RTM is a Senior Lecturer in Psychology at Leeds Beckett University. They have expertise in participatory methods and public involvement and engagement in sensitive areas (e.g., sexual harm); they will lead and manage the PPI work. SG is our PPI representative. She is a retired theatre nurse (including for gynaecology) and has lived experience of mesh complications. IR is a statistician and an expert in design and statistical analysis in clinical effectiveness studies. She will be responsible for characterising the study populations, and analysing patterns of missing data and completion rates at the questionnaire and item level. A-MB is an expert in systematic reviews, mixed methods and qualitative evidence synthesis. She will lead on the systematic reviews undertaken in WP1 and co-supervise the research fellow (60%) and research assistant (40%) at LBU.

Collaborators: JEB will provide advice on all aspects of the development of the PBM and advice around the development of the descriptive classifier used in the DCE in WP5. AM and FT are jointly leading NIHR 202450. They will collaborate with us on integrating PURSUE, and the analysis of the concept elicitation interviews in WP1. FR is the Chief investigator of the PROSPECT follow-up study and SB is the project/trial manager. They will both provide input and support to data collection and analysis/interpretation of the work planned in WP4b. All collaborators will join the project advisory group to enable them to contribute their expertise into development of the PROM.

17. Project Management, Quality Control and Assurance

This study will be conducted in accordance with the UK Framework for Health and Social Care Research. Leeds Beckett University (LBU) is the study sponsor. Lead applicant (GLJ) will take responsibility for the overall management of the project. She has been costed at 30%. Joint lead (SJ) has also been costed in at 10% ensuring there will be 2 days per week dedicated to the delivery of this programme. They will correspond as often as necessary by phone, email and video links to ensure successful project delivery against the Gantt chart and to troubleshoot if needed.

Two committees will govern the conduct of this study.

Project Management Group (PMG): This will comprise the full-time Research Officer and Research Fellow/s based at LBU who will undertake the daily running of the study, supervised by GLJ. They will meet weekly. SJ and the PPI lead will join them fortnightly to ensure efficient delivery of the study. These meetings will be in person or virtual as needed.

In addition, there will be quarterly half-day meetings in each year with the study team and PMG to ensure successful progress against the Gantt chart and identify opportunities for dissemination, and outputs.

Project Steering Committee (PSC): As a minimum, the PSC will consist of a neutral chair with PROMs and/or clinical and research expertise in urogynaecology surgery, a statistician, a patient representative and GLJ. The Committee will meet at least annually from the start of the study.

Project monitoring procedures and site monitoring will be undertaken at a level appropriate to a risk assessment performed by the sponsor or their delegate. Data Protection Impact Assessments/data management plans will be completed in collaboration with the Leeds Beckett Information Governance and IT Security teams to ensure data is processed and stored in accordance with GDPR and the Data Protection Act (2018). The study Gantt chart will be circulated to all study team members at the start of the study. Half-day training workshops will be offered to the PPI panel at the start of the six work packages to help develop their skills and knowledge of the methods being undertaken.

Finally, a **Stakeholder Consultation Group (SCG)** will also be convened. Whilst this group will not be directly involved in project management or auditing, the members will be involved in the development of the PROM. At the start of the study, the SCG will be established comprising the collaborators and key stakeholders mentioned in WP2 (2a). Along with the study team and PPI panel, they will meet once a year in the annual team meetings, with another taking place in Yr 2 and Yr 3. Members of the SCG working on specific work packages related to their specific expertise are likely to join some of the quarterly team meetings too.

18. Patient and Public Involvement (PPI)

18.1 Aim

The aim of establishing a PPI panel is to obtain guidance and feedback on the planning, delivery and dissemination of the APPRAISE study from people with lived experience of surgery for POP, SUI or mesh complications and associated QoL impacts.

18.2 Description of the Patients to be Involved

PPI Lead RTM and lived experience co-applicants SG and JH will deliver activities with 8 PPI members: 4 women from the Reproductive Health Research Public Advisory Panel in Sheffield, and to increase diversity, 4 ethnically diverse women from the Women's Voices of the Royal College of Obstetricians and Gynaecologists. PPI members will be embedded into the project to enable benefit from consultation and collaboration with diverse lay experts. RTM will manage the PPI activities, feeding back at Project Management Group meetings. RTM and SG will design and deliver the activities. The Project Officer will recruit PPI members, assist in drafting documents (e.g. induction packs), administration, minuting meetings and analysing impact assessment data. An optional private Facebook group for PPI members will assist with team-building, sharing project updates and peer support.

18.3 Support for PPI Members

Support for PPI members will include:

1) 1-day briefing and 3 days' training to ensure meaningful contributions to the project, and skill and knowledge development.
2) Paying PPI members for preparation and attendance at meetings and training events, as per the NIHR's Centre for Engagement and Dissemination's payment policy to recognise their time and contribution.
3) Delivering activities online where possible to minimise inconvenience for PPI members. (4) Costing for potential PPI access needs (e.g. language, sight/hearing).

18.4 Evidencing Impact

Evidencing impact will be achieved through:

1) An informal evaluation of PPI activities at each meeting (recorded via meeting minutes);
2) Formative and summative impact assessments, co-designed with PPI members. Formative assessments will be every 6 months to enable process improvements; the summative assessment will be at project end to demonstrate the impact of PPI (e.g. in PROM development). RTM and SG will co-write a summative report adhering to GRIPP2 (short form) guidelines.

18.5 Summary of PPI Activities

Activities include:

- 1-day in-person briefing at project start with team-building and co-design of impact assessments;
- 6 half-day online training sessions (1 per WP, by WP lead);
- 8 2-hour online PPI meetings; 1-day in-person workshop in WP2;
- 1-day in-person meeting at the project end for summative impact assessment, dissemination and project sustainability.

PPI members will contribute to every WP:

- All WPs: co-develop participant-facing materials; advise on recruitment and ethical issues.
- WP1: help plan and deliver the systematic reviews, as per Cochrane guidance (Pollock et al., 2018); review interview schedules and early findings to shape the analysis and report for WP2 participants.
- WP2: Feedback on items, format and implementation barriers of draft PROM; review participant feedback from cognitive debriefing interviews and assist in PROM modifications.
- WP3 & 4: Review the missing data analysis for the surveys to decide if items should be included in the EFA and changes to the item pool and domain structure after CFA.
- WP5: Review preference-based items for face validity and co-produce task instructions.
- WP6: Review interview schedules and early findings to shape the analysis and implementation guide.

PPI members will contribute to dissemination:

- PPI will advise on WP and PROM dissemination;
- Co-develop outputs (e.g. infographics, YouTube video);
- Co-present the YouTube video at the UK Public Engagement and Performance Conference;
- Cco-produce patient-facing documentation for the PROM.

19. Methods of Dissemination

19.1 Outputs

We will produce:

- The APPRAISE PROM to be made freely available for publicly funded use and research in clinical effectiveness studies, in both paper and electronic formats.
- A preference-based version of the PROM for use in economic evaluations.
- A published study protocol.
- A concept elaboration document to support ease of translation of the PROM into different languages.
- A dedicated project website hosted at Leeds Beckett University.
- Infographics for circulation across social media – targeted at patients and healthcare professionals. A YouTube video to provide a layperson's summary of the project findings.
- Publications from each of the six work packages in high-impact open access journals, and clinical practice guidelines (e.g., RCOG, NICE).
- Conference presentations for national and international academic, clinical and patient audiences.
- A user manual to facilitate the use of the APPRAISE PROM to enable all women to self-report the impact of pelvic floor surgery upon their QoL.
- Open access data arising from the individual work packages planned in this programme of work.

19.2 Dissemination

To actively engage and communicate with the end-users of our PROM, we will co-develop and psychometrically test the PROM in partnership with our PPI co-applicant and PPI panel to ensure it is patient-centred and meets their needs. We will disseminate the outcomes of each work package to patients and healthcare professionals as they are completed using plain English language targeted outputs for each of these audiences. These will include infographics and newsletters that will be circulated via a dedicated project Twitter account, professional societies (e.g. BSUG) and dedicated research project webpage. We will engage with third sector organisations e.g., Health Talk (www.healthtalk.org) who have already agreed to include links to our PROM on their website. We will produce a YouTube video using subtitles and audio description to explain how we developed the PROM, how patients co-developed this with us, what it is used for and how it works - content all informed by PPI. We will present at patient focused, clinical and academic conferences to disseminate our work such as the International Urogynaecology Association Annual conference, the BSUG national conference, ISOQOL and the national PROMs conference. We will liaise with our institutional press office, and those more widely e.g., at NHS England, NICE and NHS digital to create news stories for their websites, and we will disseminate the study at key milestones via the mainstream media.

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20. Costing the Project

20.1 Service Support Costs

There are service support costs for consultant and research nurse time to facilitate the identification of eligible patients (30 minutes per patient) and obtaining consent for the university staff to contact their patients (30 minutes per patient). This time is needed to achieve our optimal NHS total sample size (n=937) and also any potential non-response (estimated at 30%), whereby up to n=1277 patients might need to be approached. It also includes informed consent from hospital staff to take part in interviews.

20.2 Treatment Costs (Cost of the Procedures)

As this project focuses on PROM development, there are no treatment costs associated with this study.

21. Funding Source

This study is funded by the National Institute for Health Research NIHR Health Technology Assessment (HTA) programme (project reference number NIHR152187).

22. NIHR Portfolio Status

Portfolio status is being sought for individual work packages where relevant.

23.Department of Health and Social Care Disclaimer

The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health and Social Care.

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