STU-SOP-DMS-006 – Standard Operating Procedure on Patient Reported Outcome Measures (PROMs)

1. Purpose and Definitions

The purpose of this SOP is to describe procedures for the use of Patient Reported Outcome Measures (PROMs) in research projects and other rigorously designed studies, covering:

- Assessment of whether PROMs are to be included
- Adaptation, development, testing and validation of PROMs, where appropriate
- Collection of PROM data
- Analysis, interpretation and write up of findings related to PROMs
- Quality assurance

Definitions	
Patient Reported Outcome Measure	"Any report of the status of the patient's health condition that come directly from the patient, without interpretation of the patient's response by a clinician or anyone else[1]

2. Background

Careful choice of outcome measures is critical for evaluating the effects of any intervention. In the field of healthcare, these may include clinical measures such as survival and measures of physiological status. However, in order to understand the effectiveness of interventions from the participant's perspective, PROMs are often used alongside clinical outcomes. The US Department of Health and Human Services Food and Drug Administration have issued guidance on the review and evaluation of PROMS[1] and the European Medicines Agency issued a reflection paper to guide the use of Health Related Quality of Life (HRQL) measures in trials[2].

Recent initiatives including "COSMIN" (COnsensus-based Standards for the selection of health Measurement INstruments https://www.cosmin.nl/index.html) have attempted to standardise the use of terms and definitions in the literature on measurement properties and have issued a checklist for the critical appraisal of the validity of PROMS[3-8]. In addition, in 2013 a Patient-reported extension to the CONSORT statement was published which issues guidance regarding the reporting of PROMs outcomes from trials[9].

The Department of Health refer to PROMs as self-completion questionnaires administered to patients to assess their self-reported health status[10]. STU have broadened the concept to cover where research participants may not necessarily be patients, and also to cover any outcomes reported directly by research participants or in some cases their proxies. These could include generic or disease-specific quality of life, well-being, disease severity, social inclusion,health status or patient experience.

3. Roles and Responsibilities

Any individual within STU or collaborators involved in the selection, development, administration, recording, analysis or interpretation of PROMs has a responsibility to use this SOP.

Chief Investigator (CI) is responsible for all aspects of the research project, including ensuring that that PROMs expertise is available within the research project team.

Trial Development Group (TDG) includes service users involved in initial discussions about the viability of a research idea and selection of PROMs. For other research project designs, this may be a group with similar functions.

Trial Statistician (**TS**) offers advice on the design of the research project and is responsible for the statistical analysis plan including reporting of any PROMs.

PROMs Specialist is a member of the research project team, where required, (who may or may not be a member of the STU staff) who has specific expertise in identifying, adapting, administering, analysing and interpreting PROMs.

Data Manager (DM) is responsible for the collection and validation of research project data, including PROMs using an appropriate data management system.

Trial Manager (TM) is responsible for the oversight of the PROM process

Health Economist, where needed, will be responsible for economic evaluation within research projects, and will work closely with the PROMs Specialist in selecting appropriate PROMs to ensure that outcomes related to cost effectiveness are feasible, appropriate and undertaken to high standards of rigour.

External use of SOP: this SOP and Associated Documents (AD) may be used for research projects not adopted by STU where Swansea University (SU) staff and associated NHS organisations require guidance. In such instances, oversight responsibility for any associated tasks will not be the responsibility of STU.

4. Procedure

4.1 Pre-Project Planning

Investigators developing a research project will set up a TDG, or equivalent, (as specified in STU-SOP-TS-003 Research Project Operational Committees). A PROMs specialist should attend meetings and establish the PROMs considerations for the project as listed in PROMs Considerations (STU-AD-FRM-013). If the PROM is a primary outcome in the project, the PROMs Considerations form must be completed. The PROM specialist should draw on appropriate resources when determining if an appropriate PROM exists and when compiling a list of possible candidate PROMs. These may include reviews (e.g. Bowling[11]) and the online Patient-reported Outcome and Quality Of Life Instruments Database, ePROVIDE™ (https://eprovide.mapi-trust.org/), database searches of existing PROMs systematic reviews using the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) (https://www.cosmin.nl/tools/database-systematic-reviews) and International Consortium for Health Outcome Measurement (ICHOM) https://www.ichom.org/, for example.

4.2 Systematic review of existing PROMs

It is possible that in the course of trying to determine if any available PROMs exist, that a number of possible 'candidate' PROMs are identified. If appropriate the team should consider undertaking a systematic review of existing measures to determine the quality of the measures and the extent to which they have been validated. This will need to be appropriately resourced, either prior to, or as part of the main study. The COSMIN guidelines (https://www.cosmin.nl/tools/guideline-conducting-systematic-review-outcome-measures/) should be followed when undertaking a systematic review of PROMs. The outcome of the

review may aid in selecting an appropriate PROM.

4.3 Review nature of measurement issues to be resolved

If a decision is made by the TDG, or equivalent committee, to use a PROM, the PROMs specialist should formulate a list of potential PROMs along with any outstanding measurement issues which will then be discussed further with the TDG. The TDG will decide upon the preferred methodological approach which will be factored into the research project design:

4.2.1 PROM available with no adaptation required for present project population

When there is a PROM available where no adaptation is required for the present research project population, the PROMs specialist will check the licensing conditions and ensure that the correct version of the chosen PROM is used in the research project e.g. EQ-5D, SF-12.

4.2.2 Published PROM available but requires some adaptation for the present project

If available PROMs have to be adapted in some way (e.g. to a specific illness or population), adaptation should be carried out according to the procedures below.

4.2.3 No appropriate PROM available for measuring an outcome of the current research project – a new measure has to be developed

Resources needed for developing any new PROM must be factored into the project plan and adequate time allowed to develop PROM before the main research project or through a concurrent validation process as part of the main research project.

Any new outcome measure should be developed and validated according to general principles outlined by Streiner, Norman and Cairney[12] and and COSMIN (**https://database.cosmin.nl/**).

4.3 Finalisation of PROM data collection mechanisms

The PROMs specialist will work with the TS and the DM to ensure all identified and agreed PROMs will be gathered for analysis according to the Statistical Analysis Plan (STU-SOP-DMS-005 Creating a SAP).

PROM data collection instruments will be finalised and signed off by the Trial Management Group (TMG) as part of the research project data management process. The PROMs specialist will also provide support to the individual responsible for obtaining required approvals for the research project to ensure that all PROMs are incorporated into the appropriate application forms.

4.4 Analysis Plan

The plan for analysing PROM data should be described in the SAP developed according to STU-SOP-DMS-005 Creating a SAP.

PROM missing data should be handled according to the available PROM developers/licensing instructions. When these instructions are not available, the PROMs specialist will liaise with TS and DM to develop appropriate procedures in consultation with the TMG, and as part of the overall analysis plan. (STU-SOP-DMS-005 Creating a SAP).

4.5 PROM data collection

The PROMs specialist shall work with the TS and the DM to make sure all data collection instruments are in place, to set up and pilot detailed data acquisition and management processes. PROM data will usually be stored with all other research project data in a single data management system.
The principal objective with PROMs should always be to collect reliable, valid and unbiased data in a timely manner and within the given resource constraints without unnecessary burden

to participants. PROM data should be collected as per the ethics approved protocol.

4.6 Handling and Storage of PROM data

The TM and PROMs Specialist will ensure that all PROM data are handled and stored as described in the protocol.

4.7 Advice on analysis, interpretation and dissemination of PROM data

The PROMs specialist, where appropriate, will support the TS to analyse the PROM data.

The PROMs specialist should be involved in writing the PROM findings according to the agreed publication plan and the appropriate reporting guidelines such as CONSORT[9].

When PROMs have to be designed or adapted, it is good practice to report on the validation work through peer reviewed publication to ensure proper implementation and dissemination of the PROM.

5. References

1. U.S. Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research (CDER), et al. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Available from: https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf 2009 [accessed 5 November 2019].
2. European Medicines Agency. Reflection paper on th regulatory guidance for the use of Health-Related Quality of Life (HRQL) measures in the evaluation of medicinal products. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/reflection-paper-regulatory-guidance-use-healthrelated-quality-life-hrql-measures-evaluation_en.pdf 2005 [accessed 5 November 2019].
3. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. Qual Life Res 2010;19(4):539-49. doi: 10.1007/s11136-010-9606-8
4. Mokkink LB, Terwee CB, Patrick DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. J Clin Epidemiol 2010;63(7):737-45. doi: 10.1016/j.jclinepi.2010.02.006
5. Mokkink LB, de Vet HCW, Prinsen CAC, et al. COSMIN Risk of Bias checklist for systematic reviews of Patient-Reported Outcome Measures. Qual Life Res 2017 doi: 10.1007/s11136-017-1765-4
6. Terwee CB, Dekker FW, Wiersinga WM, et al. On assessing responsiveness of health-related quality of life instruments: guidelines for instrument evaluation. Qual Life Res 2003;12(4):349-62.
7. Terwee CB, Prinsen CAC, Chiarotto A, et al. COSMIN methodology for evaluating the content validity of patient-reported outcome measures: a Delphi study. Qual Life Res 2018;27(5):1159-70. doi: 10.1007/s11136-018-1829-0
8. Prinsen CAC, Mokkink LB, Bouter LM, et al. COSMIN guideline for systematic reviews of patient-reported outcome measures. Qual Life Res 2018 doi: 10.1007/s11136-018-1798-3

9. Calvert M, Blazeby J, Altman DG, et al. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. JAMA 2013;309(8):814-22. doi: 10.1001/jama.2013.879

10. Department of Health. Guidance on the routine collection of Patient Reported Outcome Measures (PROMs). For the NHS in England 2009/10 (Available from https://www.racp.edu.au/docs/default-source/default-document-library/guidance-on-the-routine-collection-of-patient-reported-outcome-measures-%28proms%29-%28pdf-1184-kb%29-nhs-%282008%29.pdf?sfvrsn=4) (Access date 13/03/2017), 2008.

11. Bowling A. Measuring Health: A Review of Quality of Life Measurement Scales. 3rd ed. Oxford: Open University Press / McGraw Hill 2004.

12. Streiner DL, Norman GR, Cairney J. Health measurement scales. A practical guide to their development and use. 5th ed. Oxford: Oxford University Press 2015.

6. Associated Documents

Number	Title	Location
STU-AD-FRM-013	PROMs Considerations	Q-Pulse

7. Abbreviations

List of Abbreviations	
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials
CTIMP	Clinical Trial of an Investigational Medicinal Product
DM	Data Manager
HRQL	Health Related Quality of Life
PROM	Patient Reported Outcome Measure
SOP	Standard Operating Procedure
STU	Swansea Trials Unit
TDG	Trial Development Group
TM	Trial Manager
TMG	Trial Management Group
TS	Trial Statistician
SAP	Statistical Analysis Plan

8. Appendices

Appendix 1: Document History

Version No:	3	**Effective Date:**	22-Apr-2024
Description of changes:	Updated to SOP Template v5 Addition of systematic review of existing PROMs		

Appendix 2: PROM Flowchart