BEST PRACTICE FOR IMPLEMENTATION OF PATIENT REPORTED OUTCOMES IN REAL WORLD EVIDENCE GENERATION

by

KONRAD MARUSZCZYK

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Centre for Patient-Reported Outcome Research (CPROR)
Institute of Applied Health Research
College of Medical and Dental Sciences
University of Birmingham

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Abstract

Real world evidence (RWE) plays an increasingly important role within global regulatory and reimbursement processes. RWE generation can be enhanced by collecting and using patient reported outcomes (PROs). They offer valuable insights into the long-term effectiveness, safety and tolerability of treatments from the patient's perspective. Since RWE is not limited by the constraints of randomised controlled trials (RCTs), it can provide a more generalisable picture of how therapies work in real world target populations. Additionally, collecting data during routine clinical care allows researchers to reach patient groups who might be hesitant to participate in traditional clinical trials.

However, collecting PROs in real world settings presents challenges for researchers. The doctoral research constituting this thesis aimed to identify these challenges, characterise the use of PROs in RWE generation, and seek opportunities to successfully implement PROs into real world studies. A mixed-methods approach, comprising a systematic review, quantitative analysis of current practice and qualitative interviews, was adopted to address the overall aims of this research.

Firstly, a systematic review was conducted to identify and summarise existing guidance for using PROs in RWE generation. Seven publications met eligibility criteria and were included in the review. They provided some level of guidance, addressing the following issues: PROM selection, participation and engagement, burden to health care professionals and patients, stakeholder collaboration, education and training, and implementation process. My review demonstrated that current guidance is fragmented and that no international guidelines directly address the use of PROs in RWE generation.

A quantitative analysis of ClinicalTrials.gov database records followed the review. This workstream aimed to characterise the current and past use of PROs among real world studies. Descriptions of phase IV trials were searched using an automated computer algorithm to identify studies which utilised PROs. 21% of phase IV studies between 1999 and 2021 assessed PROs. A steady increase in the utilisation of PROMs in phase IV trials has also been observed in recent years. These results suggest the potential underutilisation of PROs in phase IV trials compared to earlier phases of clinical investigations.

Finally, interviews with international stakeholders were conducted to gain deeper insights and identify challenges and opportunities for collecting and using PROs for RWE generation. Twenty-three semi-structured online interviews were conducted with patients, patient advocates, regulators, payers, clinicians, academic researchers, and industry experts. While participants acknowledged the potential of PROs in RWE generation, they also expressed mixed confidence in their value. Two types of barriers hampering the full implementation of PROs in RWE generation were identified: operational and methodological.

This doctoral research has underscored the promise of PROs in the RWE generation. Nevertheless, it also emphasised the need for further research to fully unlock their potential. Currently, a limited pool of available guidance and recommendations supports the use of PROs for RWE generation. Collaborative efforts among various stakeholders are needed to establish best practices and generate practice-changing examples of its use.

Dedication

To my dear wife – for your love, support and always being there for me!

To my amazing kids for your sunshine smiles and laughter!

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Thank you to my funder, GSK plc, for supporting my work and allowing me to research this vital topic.

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To the invaluable patient partners: A special thank you to all of you who brought your unique perspectives and lived experiences to every stage of this project. Your contributions were essential in ensuring the research remained relevant and impactful.

Finally, to my incredible family: My heartfelt thanks go to my wife, parents, and mother-in-law for their unwavering support throughout this journey. Your willingness to care for our children during long research hours allowed me to focus on this important work.

Authorship statement

The research presented in this thesis was conducted by me (KM), assisted by continuous guidance from my supervisors: Prof. Melanie Calvert (MC), Assoc. Prof. Olalekan Lee Aiyegbusi (OLA), Dr Thomas Keeley (TK) and Dr Christel McMullan (CM). Patient and public involvement (PPI) was a vital component of my doctoral research. Mr Philip Collis, a patient partner, contributed throughout my doctoral research programme by sharing his valuable lived experience and the patient perspective. Specific contributions to each paper included in this thesis are detailed below:

- A systematic review of guidance (Chapter 3) – KM, MC, OLA and TK designed the study. KM and Dr Barbara Torlinska searched databases, selected eligible publications, and extracted data. KM drafted the manuscript, which was then reviewed, edited and critiqued for intellectual content by all authors.
- Analysis of ClinicalTrials.gov records (Chapter 4) – KM, MC, OLA, and TK conceived and designed the study. Prof. Georgios Gkoutos, Dr Victor Roth Cardoso (VRC) and Dr Luke T Slater developed a matching algorithm. KM and VRC curated data and performed the analysis. KM drafted the manuscript, which was then reviewed, edited and critiqued for intellectual content by all authors.
- A qualitative study (Chapter 5) – KM, MC, OLA, TK and CM conceived and designed the study. KM conducted all interviews and transcribed them. KM coded and analysed all transcripts with secondary coder CM. Dr Catherine Bottomley and Roger Wilson contributed to data analysis during the triangulation exercise.

KM drafted the manuscript, which was then reviewed, edited and critiqued for intellectual content by all authors.

- Comment paper (Chapter 6) – The paper was conceived and designed by KM, MC, OLA, TK and CM. KM drafted the manuscript, which was then reviewed, edited and critiqued for intellectual content by all authors.

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List of abbreviations

CADTH	Canadian Agency for Drugs and Technologies in Health
CAT	Computerised adaptive testing
CFIR	Consolidated Framework for Implementation Research
ClinRO	Clinician Reported Outcomes
COA	Clinical outcome assessment
CONSORT	Consolidated Standards of Reporting Trials
EHR	Electronic health record
EMA	European Medicines Agency
EMBASE	Excerpta Medica Database
EPIS	Evidence-Based Practice Implementation in Public Service Sectors
ePRO	Electronic patient reported outcome
EU	European Union
FDA	US Food and Drug Administration
HCP	Healthcare professional
HRQoL	Health-related Quality of Life
HUI	Health Utility Index
ICTRP	International Clinical Trials Registry Platform
ISOQOL	International Society for Quality of Life Research
ISPOR	International Society for Pharmacoeconomics and Outcomes Research
JPRO	Journal of Patient-Reported Outcomes
MEDLINE	Medical Literature Analysis and Retrieval System Online
MHRA	Medicines & Healthcare Products Regulatory Agency
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
NMPA	National Medical Products Administration
ObsRO	Observer reported outcome
PCORI	Patient-Centered Outcomes Research Institute
PerfO	Performance outcome
PFDD	Patient-focused drug development
PMDA	Pharmaceuticals and Medical Devices Agency
PPI	Patient and public involvement
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PRO	Patient reported outcome
PRO-CTCAE	Patient Reported Outcomes-Common Terminology Criteria for Adverse Events
PROM	Patient reported outcome measure

PROMIS	Patient-Reported Outcomes Measurement Information System
PROQOLID	Patient-Reported Outcomes and Quality of Life Instruments Database
PROSPERO	International prospective register of systematic reviews
PROTEUS	Patient-Reported Outcomes Tools: Engaging Users and Stakeholders
QALY	Quality adjusted life years
R&D	Research and development
RCT	Randomised controlled trial
RE-AIM	Reach, effectiveness, adoption, implementation, and maintenance model
RW	Real world
RWD	Real world data
RWE	Real world evidence
RW-PRO	Real world patient reported outcome
SF-36	36-Item Short Form Survey
SFDA	Saudi Food and Drug Administration
SISAQOL	Setting International Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials
SwissMedic	Swiss Agency for Therapeutic Products
TDF	Theoretical Domains Framework
TFA	Sekhon’s Acceptability Framework
TFDA	Taiwan Food and Drug Administration
TGA	Therapeutic Goods Administration
US	United States
WHO	World Health Organisation
WHOQOL	World Health Organization Quality of Life

Formatting

This thesis was formatted according to the University of Birmingham's "Alternative Format Thesis Guidelines", which allows the inclusion of published articles as well as chapters formatted for submission to peer-reviewed journals. Full regulations are available at:

https://intranet.birmingham.ac.uk/as/studentservices/graduateschool/documents/public/rsa/alternative-format-thesis-guidelines.pdf

The work presented and discussed within the body of the thesis includes three peer-reviewed publications (KM as lead author). The publications are:

Chapter 3: Maruszczyk, K., et al., Systematic review of guidance for the collection and use of patient-reported outcomes in real-world evidence generation to support regulation, reimbursement and health policy. Journal of Patient-Reported Outcomes, 2022. 6(1): p. 57. https://doi.org/10.1186/s41687-022-00466-7

Chapter 4: Maruszczyk, K., et al., Implementation of patient-reported outcome measures in real-world evidence studies: Analysis of ClinicalTrials.gov records (1999–2021). Contemporary Clinical Trials, 2022. 120: p. 106882. https://doi.org/10.1016/j.cct.2022.106882

Chapter 5: Maruszczyk, K., et al., Paving the way for patient centricity in real-world evidence (RWE): Qualitative interviews to identify considerations for wider implementation of patient-reported outcomes in RWE generation. Heliyon, 2023. 9(9): p. e20157. https://doi.org/10.1016/j.heliyon.2023.e20157

Chapter 6 also includes a comment article submitted for publication in the peer-reviewed journal Nature Reviews Drug Discovery.

Please note:

- The pagination of the included articles is not included in the pagination sequence of the thesis submission.
- Each included article is formatted to meet journal requirements and follows the journal referencing style.
- Tables, boxes and figures are presented within the text for the reader's ease.
- Reference lists are included at the end of each chapter.
- Incorporating publication-style chapters in the thesis will inevitably lead to some duplication since each publication-style chapter will have self-contained components that will overlap with parts of the other sections of the thesis.

Chapter 1: Introduction and background

1.1 Introduction to the research

The research presented within this thesis investigates the use of patient reported outcomes (PROs) in real world evidence (RWE) generation. This chapter provides a background for this topic, justification for the research, and sets out the thesis's aims, objectives and structure.

1.2 Background

1.2.1 Outcome assessments

In life science, research studies gather measurements of different aspects of participants' health status to investigate health interventions of interest.[1] These measurements are called outcome assessments. There are three main types of outcome assessments: mortality, biomarkers and clinical outcome assessments (COAs).[2]

As defined by The International Society for Pharmacoeconomics and Outcomes Research (ISPOR) PRO Good Research Practices Task Force, COAs "include any assessment that may be influenced by human choices, judgment, or motivation".[3] By considering the person whose judgment can influence the measurement, four types of COAs are distinguished: PROs, clinician reported outcomes (ClinRO), observer reported outcomes (ObsRO), and performance outcomes (PerfO). Brief descriptions of each type of COA are provided in Figure 1.1.

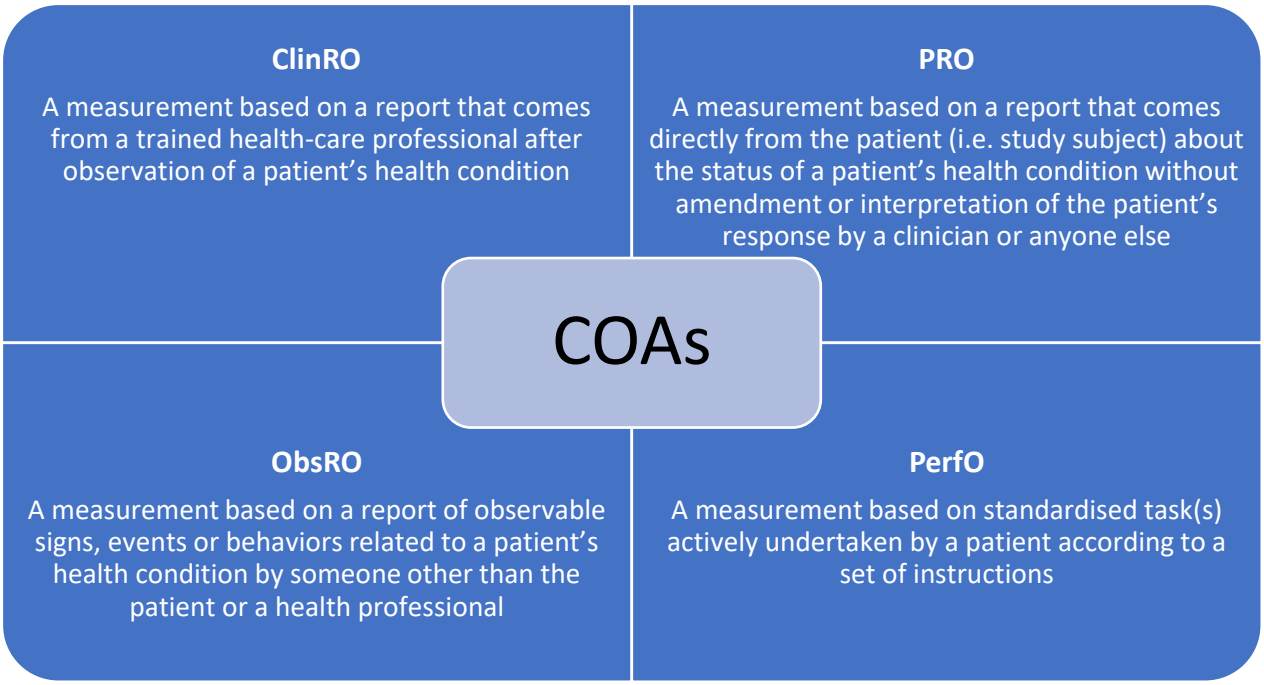

Figure 1.1. Types of clinical outcome assessments. Adapted from Walton et al. (2015).[3]

1.2.2 Patient reported outcomes (PROs)

The US Food and Drug Administration (FDA) defines a PRO as "any report of the status of a patient's health condition that comes directly from the patient, without interpretation of the patient's response by a clinician or anyone else".[4-8] PROs can assess a variety of health-related concepts [9], but most commonly, they provide information about patients':

- symptoms – signs of disease, physical or mental disturbance;
- functional status – the ability to perform various activities; and
- health-related quality of life (HRQoL) – multidimensional summary of global well–being.

PROs can provide a more comprehensive assessment of patients' health status and promote patient-centredness in life science research and healthcare provision.[10-14] A strong emphasis on putting patients at the centre of the drug development process was expressed in the US legislation – the 21st Century Cures Act.[15] It was followed by the FDA Patient-Focused Drug Development (PFDD) Guidance Series [16], which includes four documents that provide advice on the incorporation of patients' voices in medical product development. Similarly, a growing emphasis on patient involvement in life science research and development (R&D) can be observed globally.[17] For example, The European Medicines Agency (EMA) acknowledges the role of PROs in regulatory decision-making in one of its guidance documents.[18] Moreover, the EMA has recently held a workshop to explore how PROs are being used worldwide to assess anti-cancer treatments.[19]

1.2.3 Patient reported outcome measures

In research and clinical practice, PROs are usually measured using validated questionnaires, known as Patient Reported Outcome Measures (PROMs). PROMs may consist of numerous items. To ensure clarity, each item should be precise and focus on a single concept of interest.[20] The concept of interest describes "the aspect of individual's experience or clinical, biological, physical, or functional state the PROM is intended to capture".[21] Avoiding asking about multiple aspects of health within one item improves clarity and helps to provide accurate information about the specific concept of interest being assessed.

1.2.3.1 PROMs' validity

PROMs are considered fit for purpose when "the level of validation associated with an instrument is sufficient to support its proposed use".[22] US FDA listed several considerations for claiming that the PROMs are fit-for-purpose.[21] These considerations are presented in Box 1.

Box 1. FDA considerations for supporting a PROM as fit-for-purpose.[21]

1) The reason for choosing PRO to asses the concept of interest is clear.
2) All important aspects of concept of interest are covered by the selected PROM.
3) Respondents understand the instructions and items of the measure as intended by the PROM developer.
4) Scores are not be overly influenced by processes/concepts that are not part of the concept of interest.
5) The methods of scoring responses is appropriate for assessing the concept of interest.
6) Scores correspond to the specific health experiences the patient has related to the concept of interest.
7) Scores are sufficiently sensitive to reflect clinically meaningful changes within patients over time in concept of interest within the context of use.
8) Differences in scores are interpreted and communicated clearly in terms of the expected impact on patients' experiences.

Validation of the PROM is an ongoing exercise and should not be considered as concluded after the development phase is over. PROMs should be reviewed and amended if needed over their life span to address any arising challenges, e.g. language or patient experience issues.[20]

1.2.3.2 Development and validation of PROMs

PROMs are developed in a complex process using both qualitative and quantitative methods.[20] Initially, researchers gather input from the existing literature, patients and

experts to better understand the disease of interest. Also, any existing patient subpopulations characterised by distinct disease trajectories are identified. Collected information is then used to define the concept of interest. Moreover, the context of use of the PROM should be defined.[22]

The generation of items can be informed by: input obtained from various stakeholders, how relevant concepts were previously assessed in existing PRO measures and by considering the recall period and possible response options.[20] The recall period should be long enough to capture patients' experiences of interest but short enough to demonstrate the variation in patients' health over time and not overburden the responders.[23, 24] Response options to each item should be selected to best discriminate between future respondents.[20] Additionally, questions and instructions should be worded in plain language without medical jargon. Careful attention should also be paid to the translation and cultural adaptation of the PRO questionnaire.[25]

In-depth cognitive interviews with patients from the target population follow initial PROM development. Usually, they are asked to complete the PROMs and are interviewed by the researchers. The main aim of the cognitive interview is to assess whether the patient's understanding and interpretation of questions and response options align with the developer's intention. Interviewers also check if the questionnaire wording is understandable and culturally appropriate for the target population.[20]

As the next step, the newly developed PROM is tested within the target population. The PROM is then compared to existing ones assessing similar concepts. Various aspects of PROM are scrutinised at this stage, including their psychometric properties:

- validity – the degree to which the PROM measures the construct(s) it claims to measure;
- reliability – the degree to which PROM is free from measurement error; and
- responsiveness – the ability of PROM to detect change over time.[26]

1.2.4 PROMs taxonomy

One way of categorising PROMs is to consider the scope of the measurement. PROMs can be divided into condition-specific and generic measures.[9] Condition-specific measures are designed to be used in a particular health condition or groups of conditions manifested in a similar pattern. They provide more precise information about disease progression and treatment effect than generic measures.[27] On the other hand, generic measures describe the overall picture of patients' well-being. They provide better comparability between different health conditions and are often used at the organisational or system level to inform economic models.[27, 28]

PROMs can also be categorised based on their measurement focus. PROMs can collect information on the following outcomes of interest: symptom burden (e.g. pain, nausea), overall side effect impact/tolerability, functional status (e.g. mobility, self-care) or HRQoL as a multidimensional summary of global well-being.[29]

Moreover, the type of measurement utilised can be considered. Profile or preference-based PROMs can be distinguished from each other.[29] Profile measures (e.g. SF-36, WHOQOL, PROMIS) summarise patients' responses, reporting scores on specific domains or generating single score value.[29] In contrast, preference-based PROMs (e.g. EQ-5D, HUI) yield a single index score summarising multi-domain concepts using PRO

tariffs. Tariffs are developed using various preference elicitation methods.[30] Preference-based PROMs are often used to generate utility values to inform health economics modelling and are described in more detail in section 1.2.7.3.

It is also vital to distinguish PROMs from patient reported experience measures (PREMs). As the first collects reports about respondents' health and well-being, the latter investigates patients' experiences associated with care provision, their satisfaction with received care and access to healthcare services.[31] The focus of this thesis is solely on PROs and PROMs.

1.2.5 Approaches to PRO data collection

PROs can also be characterised by how and from whom the data were collected. First, the data source should be considered. By definition, PRO should be obtained by self-reporting, unfortunately it is not always possible. In some instances, using a proxy (someone else responding about the patient's health, e.g., carer or parent) need to be considered. Self-reporting is strongly preferred by regulatory bodies as expressed in their guidance documents.[4, 32] However, a significant need for proxy reporting remains among specific patient populations, such as children or terminally ill patients.[33] In that case, it is preferable to administer observer-completed questionnaires instead of proxy completion of PROMs originally designed for self-reporting. For instance, the Pediatric Quality of Life Inventory (PedsQL) have parent versions for the younger age groups.[34] More research is needed to better understand the complexities of proxy reporting and to improve the accessibility of existing PROMs to individuals who have difficulties completing them, e.g. the one with cognitive impairment.[33]

Secondly, the mode of questionnaire administration should be distinguished. PROMs can be self- or interviewer-administered.[9] Self-administration allows patients to complete questionnaires at their own pace and can be particularly useful when questions relate to sensitive topics such as sexual health. On the other hand, when interviewers administer questionnaires verbatim, they can provide responders with additional clarification when needed or assist patients with conditions limiting their ability to fill them independently. Thus, interviewer administration can be the only option to gather PRO data among some patient sub-groups, such as those with ill health or with some forms of cognitive impairment.

Last, various administration methods can be used, including pen and paper, phone interviews, or electronic data capture such as computers, tablets or smartphones. Historically, PROMs were administrated as paper questionnaires. PRO responses were then manually entered into clinical trial databases. It was the most accessible and affordable way of collecting PRO data. With technological advancement, other administration methods have become available. Various electronic devices, including tablets, smartphones or computers, can collect electronic PROs (ePROs). ePROs have positively impacted the quality of gathered data and reduced missing data points.[35-37] They also enable the use of computerised adaptive testing (CAT). CAT selects only relevant questions based on previously obtained answers to be completed by each individual. ePROs can be collected in various settings, including in-clinic data collection and remote data submission at patients' convenience.

Numerous studies have demonstrated measurement equivalence of ePROs and traditional pen-and-paper questionnaires.[36, 38] On the other hand, it was shown that differences in settings where PROs are provided could be a source of bias (e.g. home vs in-clinic).[35] Automated phone services pose a valuable alternative to other forms of electronic data capture, especially for less technologically competent patients, those with visual impairment or those without access to the Internet.[39]

Researchers planning the study or PRO system should carefully consider the selection of an appropriate data collection method or a mix of methods. Additional research is needed to study the equivalence of alternative data collection methods.[33] Special consideration should be given to the data collection in the real world setting, where studies are particularly exposed to multiple sources of heterogeneity.

Aiyegbusi et al.[24] presented recommendations to reduce respondents' burden while collecting PROs to maximise the quality and quantity of collected data. Characteristics of the target patient group and the purpose of data collection should be carefully considered. Patient involvement is also vital for the design of successful PRO systems, including the selection of PROMs and modes of data collection.

1.2.6 PROs to promote inclusive and equitable evidence generation

Historically, health research tended to exclude participants from underserved groups.[40] Personal characteristics, including socio-demographics, education level or economic inequalities, often correlate with research participation.[40, 41] Gaining feedback from patients, including collecting PROs, poses an excellent opportunity to enhance patient engagement.[42, 43] It can be a valuable tool for engaging patient subgroups historically

suffering from systematic omission, e.g., those from minority ethnic groups who may also distrust research.[44]

On the other hand, PRO data collection methods used should aim to strengthen equity in health research and improve inclusivity.[44] Researchers should consider the target populations and carefully select data collection strategies to avoid excluding individuals from underserved groups, such as those of specific demographics (e.g. age, gender, sexual orientation or ethnic origin), social or economic characteristics (e.g. income, education level, digital literacy) or health status (e.g. pregnancy, comorbidities or cognitive impairment). Also, involving patients from different backgrounds in the study design phase increases participants' retention and engagement. Appropriate training should be offered to individuals involved in study execution to promote equitable data collection.[41, 44]

1.2.7 PROs in research

Historically, PROs, were utilised as one of the endpoints assessed in clinical trials.[45, 46] The primary purpose for their use was to generate evidence. This section will focus on the role of PRO in research. PROs' applications outside the research setting are described in section 1.2.8.

1.2.7.1 PROs to describe the burden of the disease

PROs are a valuable tool for describing the disease's burden and the illness's natural history. They can depict how the condition impacts the daily living of affected people.[11] PROs can help to combat paternalistic attitudes in health care research.[47] Various study types are used to describe the impact of the disease on patients' lives by utilising PROs,

including disease burden studies, observational studies, surveys, and natural history studies.

1.2.7.2 PROs in clinical trials

PROs are commonly used to assess the risks and benefits of treatments as part of comparative effectiveness studies.[48] PROs are increasingly being used to provide a measure of efficacy and tolerability in early phase clinical trials and effectiveness in the later phases of clinical research.[49]

A clinical trial is a rigorously designed scientific investigation involving humans.[50] It is mainly performed to determine optimal dosage and evaluate the risks and benefits of new medical interventions. Clinical trials are conducted according to carefully developed protocols and follow a structured progression (phases). Different phases aim to answer various questions and can be characterised as shown in Table 1.1. Although the traditional breakup of the clinical trial phase is presented here, some investigations undertake combined multi-phase studies.[51]

Table 1.1. Phases of clinical trials.[52]

Clinical trial	Characteristics	Aim
Phase I	Small groups of volunteers (below 100 people). The short duration of the study – below a few months.	Focused primarily on the intervention's safety, tolerability, and detection of adverse events. It also investigates the pharmacodynamic properties of the medicine and tests the dosage range.
Phase II - also referred to as proof of concept or proof of mechanism	Larger groups of participants – a few hundred. Moderate duration of the study – up to a year.	To determine the efficacy of a new intervention and further investigate its safety. To identify the optimal dose of a drug.
Phase III	Even larger groups of participants – from hundreds to thousands. Longer duration – up to a couple of years.	To confirm the efficacy of the intervention, monitor adverse events and compare them with alternative treatments. Results of phase III clinical studies are generally used to support market approval and reimbursement applications.
Phase IV	Broad, population-based studies. Long-term observations.	After the product launch, it monitors safety and informs about real world effectiveness and optimal use of interventions. Identifies rare adverse events or drug interactions.

Random assignment of participants to study arms is used in clinical trials to ensure unbiased results. Randomised Control Trials (RCTs) are the gold standard of clinical investigation. Randomisation helps to control for confounding factors – participants' characteristics which could impact study results – by distributing them by the play of chance between the groups being compared.[53]

Clinical trials to generate robust results need to demonstrate internal and external validity. The study is considered internally valid when observed differences between the groups are correctly attributed to the intervention being investigated.[54] Internal validity can be jeopardised by a study's systematic error (bias) or random error. In other words, internal validity informs whether the study was correctly executed. On the other hand, external validity refers to the ability of results to be generalisable to other circumstances outside the study itself.[54] It answers whether the result obtained in this study is meaningful to the research question in mind. Internal validity is the *sine qua non* for external validity of the study. However, not every internally valid study will demonstrate external validity.[55]

Clinical trials analyse outcome assessments of investigated groups to assess whether the intervention leads to better health results than the control group.[2] Study endpoints are specified *a priori* and can consist of various outcome assessments. They are measured at specified time points and analysed using appropriate statistical methods.[2]

A primary endpoint is the most critical measure of the study, which should be capable of answering the research question. Primary endpoints are used to calculate a sample size needed to demonstrate statistically significant differences between the groups, which is anticipated by the researchers (power analysis).[56, 57] Secondary endpoints are supportive measurements related to the primary endpoint or measurements of effects related to the secondary objectives of a trial.[56, 57] Remaining endpoints gathered as part of the trial are known as exploratory endpoints. Exploratory endpoints are usually not analysed as rigorously as primary and secondary endpoints.

Although PROs can be incorporated into any endpoint type, they are usually used as a secondary or exploratory endpoint.[58, 59] PROs are one way of assessing and evaluating the impact of interventions being compared on patients and are commonly used in clinical research along with other types of outcome assessments. PROs are beneficial for providing a more holistic view of patients' health status. They differ from other kinds of outcome assessments used in clinical trials as they depict the effects of health interventions from the patient's perspective.[11]

PROs are particularly useful in assessing the safety and tolerability of health interventions. Patient Reported Outcomes-Common Terminology Criteria for Adverse Events (PRO-CTCAE) is a PRO-based measurement system designed to evaluate symptomatic toxicity in patients receiving oncological treatment.[60] It was developed to assess and report adverse events experienced by cancer clinical trial participants from the patients' perspective. The need for assessing the tolerability of oncological treatments based on patient reported data was also reiterated in a Friends of Cancer Research White Paper.[61] Apart from the PRO-CTCAE, a single item PROM (FACT-GP5)[62] was proposed as a short and simple way of identifying burden associated with treatment's side effects experienced by patients. PROs for the assessment of tolerability of health interventions are also increasingly used in non-oncological trials. The drug is considered tolerable when patients are willing to receive it even when treatment side effects are present.[63] One example of this can be found in the study investigating treatment for patients with inflammatory conditions where a set of ePROs was used throughout the duration of the trial.[64]

Preference-based PROs captured as part of clinical trials are often used to determine the cost-effectiveness of health interventions informing reimbursement decision-making.[65] Health state utilities used in economic models are usually estimated based on PRO responses of clinical trial participants. Additional information on how PROs inform cost-effectiveness studies can be found in the section 1.2.7.3.

The implementation and use of PROs in clinical trials were the subject of several guidance documents issued by scientific groups and regulatory or reimbursement bodies.[66] Examples of key guidance documents on the use of PROs in clinical trials are presented in Table 1.2.

Table 1.2. Key guidance documents on the implementation and use of PROs in clinical trials.

Nr	Year	Title	Issuing body/working group
1	2009	Guidance for industry: patient-reported outcome measures: use in medical product development to support labelling claims[4]	FDA
2	2013	Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension[67]	The Consolidated Standards of Reporting Trials (CONSORT)
3	2013	Minimum standards for patient-reported outcome measures used in patient-centred outcomes and comparative effectiveness research[68]	International Society for Quality of Life Research (ISOQOL)
4	2016	Appendix 2 to the guideline on the evaluation of anticancer medicinal products in man: the use of patient-reported outcome (PRO) measures in oncology studies[18]	EMA

Nr	Year	Title	Issuing body/working group
5	2018	Guidelines for inclusion of patient-reported outcomes in clinical trial protocols: the SPIRIT-PRO extension[69]	Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)
6	2018	Patient-Focused Drug Development: Collecting comprehensive and representative input[70]	FDA
7	2020	International standards for the analysis of quality-of-life and patient-reported outcome endpoints in cancer randomised controlled trials: recommendations of the SISAQOL Consortium[71]	Setting International Standards in Analyzing Patient-Reported Outcomes and Quality of Life Endpoints Data (SISAQOL consortium)
8	2021	'Give Us The Tools!': development of knowledge transfer tools to support the involvement of patient partners in the development of clinical trial protocols with patient-reported outcomes (PROs), in accordance with SPIRIT-PRO Extension[72]	International experts with patient and public involvement
9	2022	Patient-Focused Drug Development: Methods to identify what is important to patients[73]	FDA
10	2022	Patient-Focused Drug Development: Selecting, developing, or modifying fit-for-purpose clinical outcome assessments[21]	FDA
11	2022	Ethical Considerations for the Inclusion of Patient-Reported Outcomes in Clinical Research: The PRO Ethics Guidelines[74]	International experts with patient and public involvement
12	2023	Patient-Focused Drug Development: Incorporating clinical outcome assessments into endpoints for regulatory decision-making[75]	FDA

1.2.7.3 PROs to inform economic evaluations

PROMs are vital for determining the cost-effectiveness of alternative health interventions. They are used to assign utility values to the health states distinguished in economic models. Although EQ-5D, SF-6D, or HUI questionnaires are commonly used for this purpose, some studies perform a direct valuation of PRO responses or map obtained PRO results to already developed utility tariffs.[76, 77] Utilities are usually expressed on a scale between 0 and 1, where 0 means “dead”, and 1 represents “full health”.[78] Some utility tariffs also allow for negative values representing health states worse than death. Utility values are assigned by performing preference elicitation experiments (direct valuation) on large groups of respondents (usually the general population or patients).[79] Thus, PROMs used to construct such tariffs are often referred to as preference-based measures. Various preference elicitation methods include visual analogue scales, standard gamble, time trade-off or discrete choice experiments.[79] A set of health state descriptions based on hypothetical responses to particular PROM are valued by responders, resulting in the development of utility tariff. PRO scores are collected among participants in clinical trials or as part of separate studies investigating HRQoL among certain groups of patients. Tariffs are then used to assign utility values to health states of interest, which will be used in economic models.[78]

Utility values are essential for quality adjusted life year (QALY) calculation.[79] QALY is a standard unit quantifying the “amount of health” generated by alternative health interventions. QALY facilitates comparison of the health consequences across the broad spectrum of health conditions. One QALY denotes one year of life in full health. They are

often used to inform reimbursement decisions made under the utilitarian approach – the paradigm promoting overall better consequences when comparing the benefits and harms of alternatives.[80] Cost-effectiveness thresholds used in reimbursement decision-making are usually determined as a price per additional QALY generated.

1.2.8 PROs collected outside the research setting

The rapid growth of health informatics infrastructure has provided large-scale PRO data collection opportunities.[81] Collecting PRO outside of the research setting became feasible as part of routine healthcare delivery.

PRO data collected as part of routine practice are used for various purposes, including:

- healthcare service improvement;
- conducting audits;
- benchmarking service providers;
- value-based care initiatives;
- informing care at the individual level and
- evidence generation.[39]

The NHS (National Health Service) Quality and Outcome Framework [82] is a voluntary reward and incentive scheme for all general practices in England. PROs are collected as part of this framework, among other data types. The scheme acknowledges practice achievement results. It is not about performance management but resourcing and rewarding good practice. Another example of PRO collection in routine practice is, initiated in 2009, the UK PROMs programme.[83] PROs are collected from patients undergoing

selected surgical procedures. Each patient receiving hip or knee replacement is invited to fill in PRO questionnaires before and after the surgery. NHS uses this information to review its care pathways, identify good practices, and influence payments for healthcare services by promoting providers who deliver better patient outcomes. Moreover, summaries of collected PRO data are being published to inform patients' choices about where to be treated. PROs are also planned to be extensively utilised across the Welsh healthcare system.[84] Introducing PROs is part of the bigger initiative promoting value-based care delivery. The new model of care implies broad PRO data collection across the healthcare system. The provided data will support the delivery of care at the individual and population levels, which will help answer some of the questions affecting the Welsh NHS.

Another example of PRO utilisation to attain efficiency gain at the healthcare system level can be found in Denmark.[85] Remotely collected PROs inform the scheduling of visits for patients with chronic conditions. PRO scores are used to discriminate patients who require urgent medical attention from those who are attaining optimal health outcomes from the current therapies, and there is no need to see them in the clinic. AMBUFLEX system has been in operation since 2012 and spans almost 70 groups of diseases.

Apart from providing benefits materialised at the health care system level, PROs are highly valuable in informing the provision of care at the individual patient level.[86] Patients' responses to PRO questionnaires can provide meaningful information to physicians. PROs can help identify the most critical health problems that should be addressed in the first place.[87-89] Collecting PROs before the medical appointment and presenting these

data to the physician can speed up the patient interview and redirect attention to particular issues. PROs can inform treatment selection and modification of the prescribed therapy. They can also identify patients with deteriorating health status and prioritise their appointments. PRO alerts enable flagging to the HCPs in real time concerning levels of patients' responses so they can be acted upon accordingly.[14] PROs can also be used to inform patient referral pathways.[90]

Several studies have demonstrated that using PROs in routine practice can improve patient-physician communication and symptom control or positively impact health outcomes.[13, 87, 91-93] However, a more recent systematic review has shown no apparent effect of PRO use on improving health in routine oncology settings.[94] Nevertheless, the review indicates some potential areas for patient health improvements, concluding that more well-reported trials are needed to investigate the impact of PRO data collection on health outcomes.

The methods for PRO data collection for routine care vary from setting to setting. Traditional pen and paper questionnaires, phone interviews and electronic data submission (in-clinic tablet, remote website, remote smartphone app) are commonly used.[39] Due to improving access to the Internet and smartphones, remote PRO submission from patients' own devices - bring your own device (BYOD) – is becoming increasingly popular.[95-97] The usefulness of this data collection method was proven during the COVID-19 pandemic when it was used for remote patient monitoring and has gained momentum since then.[98-100]

Various scientific organisations and research groups issued guidance documents to help successfully incorporate PRO into routine care delivery. Key guidance documents in this area are presented in Table 1.3.

Table 1.3. Key guidance documents on the implementation and use of PROs in routine practice.

Nr	Year	Title	Issuing body/working group
1	2015	User's guide to implementing patient-reported outcomes assessment in clinical practice[101]	ISOQOL
2	2017	Framework To Guide The Collection And Use Of Patient-Reported Outcome Measures In The Learning Healthcare System[102]	Interviews with PROMs users
3	2017	Users' Guide to Integrating Patient-Reported Outcomes in Electronic Health Records[103]	Patient-Centered Outcomes Research Institute (PCORI)
4	2019	Implementing patient-reported outcome measures in clinical practice: a companion guide to the ISOQOL user's guide[104]	ISOQOL
5	2019	A PRO-cision Medicine Methods Toolkit to Address the Challenges of Personalizing Cancer Care Using Patient-Reported Outcomes: Introduction to the Supplement[105]	Patient-Reported Outcomes Tools, Engaging Users and Stakeholders (PROTEUS Consortium)
6	2021	ePROs in clinical care. Guidelines & tools for health systems[106]	CERTAIN
7	2023	The PROTEUS Guide to Implementing Patient-Reported Outcomes in Clinical Practice: A Synthesis of Resources[39]	PROTEUS Consortium

1.2.9 Real world data and real world evidence

As mentioned in the previous section, PROs captured outside of the formal clinical trial setting can be used, among other purposes, to generate real world evidence (RWE). The FDA defines RWE as clinical evidence assessing the benefits and risks of a medical product derived from analysis of real world data (RWD) generated prospectively and retrospectively by different study designs.[107] According to the FDA, the term RWD relates to data about “patient health status and/or the delivery of health care routinely collected from a variety of sources”.[107] The most common RWD sources are: electronic health records, claims databases, registries, and patient-generated data.[107] On the other hand, the UK National Institute for Health and Care Excellence (NICE) defines RWD as “data relating to patient health or experience or care delivery collected outside the context of a highly controlled clinical trial. RWD can be routinely collected during the delivery of health or social care or can be collected prospectively to address specific research question(s). It can come from many different sources, including patient health records, administrative records, patient registries, surveys, observational cohort studies and digital health technologies.”[108]

Differences in how RWD is perceived can be much more striking than between the FDA and NICE definitions. A study that interviewed international regulators and payers revealed a lack of consensus about the acceptable sources of RWD.[109] The variety of RWD sources mentioned by study participants is depicted in Figure 1.2

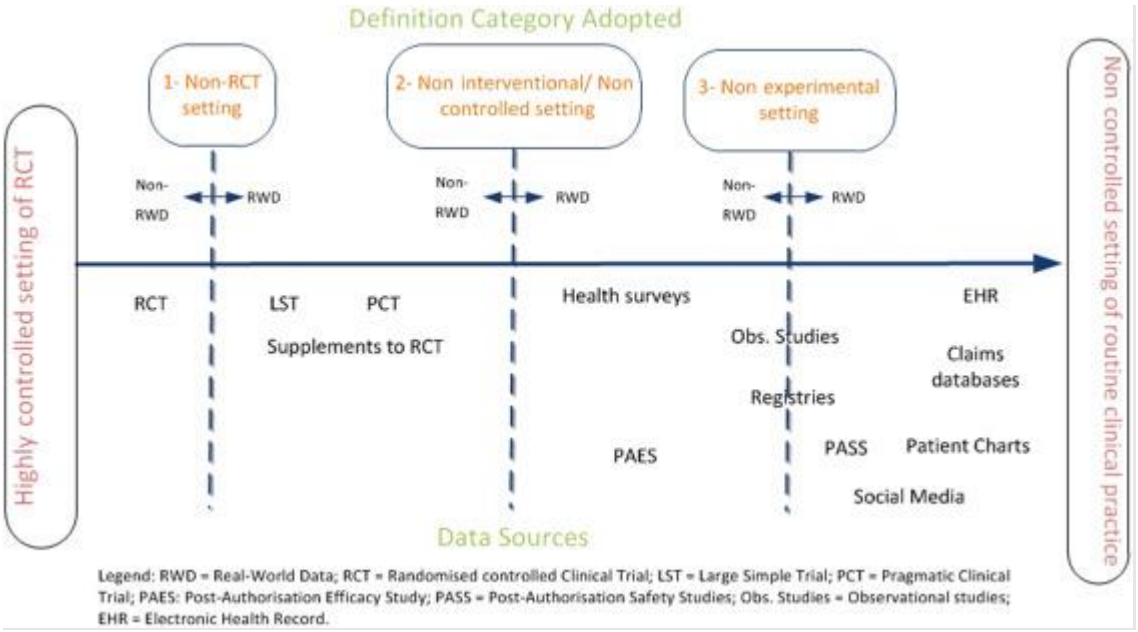

Figure 1.2. Sources of RWD. Reproduced with permission.[109]

Interviewees mentioned multiple possible RWD sources, but three main research settings in which RWE can be generated were identified: non-RCT, non-interventional/non-controlled and non-experimental. Some participants adopted a broad definition, considering any data generated outside RCT as RWD. In contrast, at the other end of the spectrum were individuals who acknowledged RWD as data solely collected in routine care delivery, e.g. from electronic health records (EHRs) or claims databases.[109]

Thus, data sources used to extract RWD constitute a continuum. Various opinions of what should be included in this set exist. An essential argument in this debate is whether patient consent is obtained to gather that data – similar to prospective studies. The need to conduct a formal recruitment process raises concerns about the participants' selection

bias and reduced generalisability of data gathered in this way when compared to routinely collected data.

RWE has already been utilised in regulatory decision-making processes, demonstrating the robustness of this type of evidence.[110] One of the first examples of such use was the label extension for tacrolimus to prevent lung transplant rejection.[111] RWE has also been used to support regulatory approval for drugs targeting rare diseases: cerliponase alfa for Batten disease[112], omaveloxolone for the treatment of Friedreich's ataxia[113] and elivaldogene autotemcel for the treatment of adrenoleukodystrophy[114].

The growing interest in RWE among regulatory and reimbursement bodies is global. Recently published RWE guidance documents and frameworks can confirm that interest. Selected documents issued by international regulatory bodies and payers focusing on RWE for their decision-making are presented in Table 1.4.

Table 1.4. RWE frameworks and selected guidance documents.

Nr	Year	Title	Country	Issuing body
1	2018	The Framework for FDA's Real-World Evidence Program[115]	US	FDA
2	2019	Guidance on Post-Market Clinical Follow-Up Studies[116]	Saudi Arabia	Saudi Food and Drug Administration (SFDA)
3	2021	MHRA guideline on randomised controlled trials using real-world data to support regulatory decisions[117]	UK	Medicines & Healthcare products Regulatory Agency (MHRA)
4	2021	MHRA guidance on the use of real-world data in clinical studies to support regulatory decisions[118]	UK	MHRA

Nr	Year	Title	Country	Issuing body
5	2021	Guideline on registry-based studies[119]	EU	EMA
6	2021	Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision Making for Drug and Biological Products[120]	US	FDA
7	2021	Guideline on Using Real-World Data to Generate Real-World Evidence[121]	China	National Medical Product Administration (NMPA)
8	2021	Guidance on Requirements When Using Real World Data/Real World Evidence as Drug Review Documents[122]	Taiwan	Taiwan Food and Drug Administration (TFDA)
9	2021	Real world evidence and patient reported outcomes in the regulatory context[123]	Australia	Therapeutic Goods Administration (TGA)
10	2021	Basic principles on Utilization of Registry for Applications[124]	Japan	Pharmaceuticals and Medical Devices Agency (PMDA)
11	2022	NICE Real-World Evidence Framework[108]	UK	NICE
12	2022	Submitting Documents Using Real-World Data and Real-World Evidence to FDA for Drug and Biological Products[125]	US	FDA
13	2022	Guideline for Communication and Exchange of real world evidence supporting drug registration applications[126]	China	NMPA
14	2023	Guidance for Reporting Real-World Evidence[127]	Canada	Canadian Agency for Drugs and Technologies in Health (CADTH)

Nr	Year	Title	Country	Issuing body
15	2023	Data Quality Framework for EU Medicines Regulation[128]	EU	EMA
16	2023	Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices[129]	US	FDA
17	2023	Real-World Data: Assessing Registries To Support Regulatory Decision-Making for Drug and Biological Products[130]	US	FDA
18	2023	Data Standards for Drug and Biological Product Submissions Containing Real-World Data[131]	US	FDA
19	2023	Swissmedic position paper on the use of real world evidence[132]	Switzerland	The Swiss Agency for Therapeutic Products (SwissMedic)

Although numerous RWE frameworks and guidance documents have been published, they do not provide PRO-specific guidance, which was demonstrated in more detail in Chapter 3. Nevertheless, some of these publications acknowledged PROs as valuable sources of RWD.[115, 123]

RWE is useful for evaluating the post-approval long-term effectiveness, tolerability, and safety of products and for informing their label expansion. RWE can also provide valuable input in the early phases of product development by characterising disease burden, depicting progression trajectories, and inputting to the design of the following stages of clinical investigation.[133] RWE studies are characterised by less stringent patient eligibility criteria than formal clinical trials. Due to that, it is possible to observe diverse, larger and more heterogeneous patient populations.[134]

Apart from informing regulatory and reimbursement decision-making processes, RWE can be a valuable source of knowledge informing delivery of care at the individual level. It can help to tailor care to the needs of individual patients. Studying RWD is especially helpful for understanding how well different treatments work in everyday medical settings among patients with similar characteristics. Some of this distinct features might not be easily represented in traditional RCTs. Information about the tolerability of treatments and adverse events experienced can be crucial when planning patient care. This information can inform patient-physician discussions, and harness shared decision-making about the treatment of choice.[43]

1.2.10 Benefits of real world patient reported outcomes

1.2.10.1 PROs vs other types of outcomes

PROs offer a more comprehensive description of health status than other outcome assessment types, e.g., biomarkers or ClinROs. They can combine multiple aspects of a person’s health into a single measure. This sensitivity makes PROs crucial for detecting safety signals, which is essential when evaluating a treatment's safety profile or tolerability. PROs can identify a broad range of symptoms that affect a patient's overall well-being. Additionally, all information captured by PROs is reported directly from the patient's perspective, which is key for defining the tolerability of investigational treatments.

Primary clinical trial endpoints often focus on specific aspects of health targeted by a treatment's mechanism, rather than the totality of a patient's health. By supplementing these efficacy measures with PROs, we can gain a more comprehensive understanding of the health effects of treatments and incorporate patients' perspectives into the

assessment of health interventions. Additionally, PROs are frequently the only feasible way to measure changes in health that are not objectively measurable, such as pain or mental health issues.

The importance of including PROs in the assessment of treatment tolerability is exemplified by iron chelation therapy for beta-thalassemia patients undergoing regular blood transfusions. Iron chelation therapy aims to remove excess iron accumulated from frequent blood transfusions. However, it can lead to significant side effects like gastrointestinal problems, renal failure, joint issues, anaemia, rash, audiological, and ophthalmological problems.[135, 136] The burden associated with these common side effects often results in treatment discontinuation.[137] Studies using patient-reported information have demonstrated a high patient and caregiver burden associated with both the underlying disease and the treatment regimens offered.[138]

Incorporating PROs into the assessment of iron chelation agents allows for a more complete characterisation of treatment effects. While the mechanism and efficacy of iron chelation are well-documented and understood, selecting a treatment regimen with an acceptable tolerability profile for individual patients remains challenging. PROs are valuable tools for depicting the impact of treatments on the overall health status of patients. A significant portion of health consequences associated with iron chelation therapy would likely be missed without the use of PROs.

PROs offer unique insights that cannot be captured by other types of outcome assessments and should be used to complement these measures in diverse study designs and settings.

1.2.10.2 Individual patient level

Once collected as part of routine care, PRO data can be utilised for multiple purposes.[139] Their benefits can be materialised at the healthcare system level and when delivering care for individual patients.[39] Figure 1.3 depicts real-world patient reported outcomes (RW-PROs) at the individual patient level (orange arrows) can inform treatment choices and strengthen patient communication. They can be used to monitor patients over time and trigger particular actions in the process of care (PRO alerts). Detecting worsening PRO scores can prioritise appointments for patients providing such information. PROs might be used to impact patient referral pathways and play a role in financing healthcare services through various value-based initiatives. Pre-specified PRO scores can trigger payments for healthcare services at a certain level to promote or penalise service providers.[140]

Utilising PROs at the individual patient level can generate efficiency gains for the entire healthcare system. For example, remote patient monitoring might help avoid unnecessary clinic appointments safely, freeing precious resources for those in need.[141]

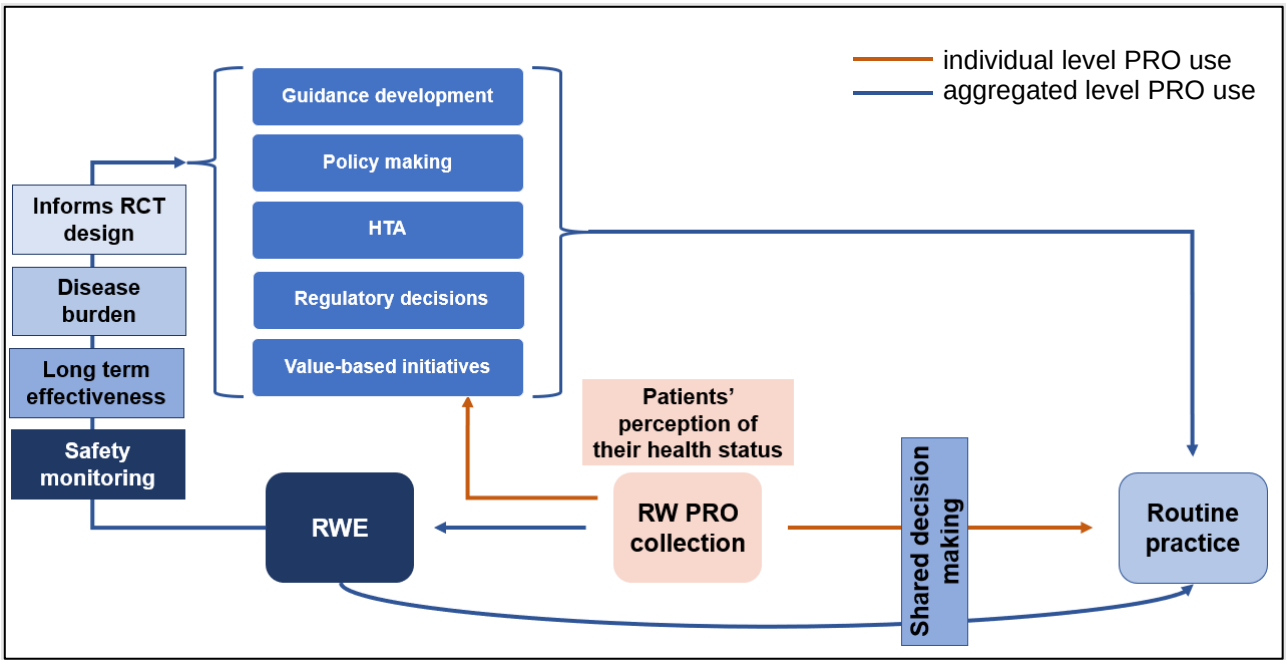

Figure 1.3. RW-PROs in the healthcare system landscape.

1.2.10.3 Aggregated level

On the other hand, RW-PROs, when analysed at the aggregated level, can be used for research (blue arrows). RW-PROs can realise all the benefits of RWE (as mentioned in section 1.2.10.1) and document it from the patient's perspective. They provide a more comprehensive picture of how patients do on treatments of interest.

RW-PROs can then be used in regulatory and reimbursement decision-making. For example, the US FDA has recently acknowledged in their guidance "Use of Real-World Evidence to Support Regulatory Decision-Making for Medical Devices" that patient experience and patient-generated data can be valuable tools to supplement data from clinical trials and can help ensure the safety and effectiveness of medical devices. The

US regulator encourages manufacturers of medical devices to collect RWD and explains how to analyse it to support their marketing applications.[129]

RW-PROs can inform the development of clinical practice guidance and health policymaking. It is often impossible to conduct experiments to evaluate the effects of health policy programs, so RWE provides promising opportunities in this space. Again, RW-PROs at the aggregated level can inform the design of value-based initiatives and healthcare resource allocation decisions by informing the reimbursement process and being incorporated into pay-for-performance schemes.[142] The collection of RW-PROs can be mandated as part of conditional coverage decisions when areas of uncertainty concerning long-term effectiveness and cost-effectiveness exist. Occasional review of post-launch data should be able to derisk investment decisions made by payers.

As shown in Figure 1.3, RW-PROs can play a central role in developing a learning, patient-centric healthcare system. PROs can strengthen the delivery of individual care. On the other hand, decisions made at the health care system level, also informed by RW-PROs, will inevitably impact routine practice. Including PROs in all these processes is an opportunity to gain more attention to the patient's perspective in making these decisions.

Another example of RW-PROs potential use is in association with tokenisation. One of the most critical challenges when gathering healthcare data is that no single data source provides the full picture of the patient’s journey. Various databases hold information about single patient: clinical trials, EHRs, lab results, prescriptions, hospitalisation episodes, and records of different payers. Merging these data is challenging, expensive and troublesome. Tokenisation allows the identification of individual patients across various

databases while ensuring that their personal details are not disclosed.[143, 144] Tokenisation allows tracking patient journeys over time. For example, it will enable the collation of deidentified healthcare data depicting all types of health services received by the patients before the initiation of the clinical trial, during the study, and to follow them many years after the study completion. Multisource health data captured with the use of tokenisation as part of routine healthcare provision has a potential to supplement clinical trials. However, additional applications of tokenisation have yet to be seen. PROs can be one of the data types that can be aggregated using tokenisation.

Healthcare systems are becoming increasingly interested in large-scale health data capture. An example of this can be found in the European Union (EU), where EMA established the Data Analysis and Real World Interrogation Network (DARWIN EU).[145] The network is designed to pull together medical information collected in routine practice from all EU countries. Its primary aim would be to inform the European regulatory decision-making process. PROs will most likely constitute one data type gathered for this initiative.

1.3 Justification for the research

As shown in the previous sections of this chapter, RW-PROs have the potential to provide numerous benefits at various levels of the healthcare system. The potential benefits of implementing PROs into RWE generation were also expressed in a commentary article by Prof. Calvert and colleagues.[146] Apart from identifying the potential advantages of RW-PROs, the authors developed a list of considerations that must be addressed to ensure their successful implementation. This paper called for shared efforts to advance the field. The work by Calvert et al. has become a cornerstone for the research presented

in this thesis. The paper establishes the need for RW-PRO research by pointing out the lack of available standards for collecting and using this type of data, which real world (RW) researchers could follow. It also highlights stakeholder interest in the topic despite limited knowledge about how to overcome numerous barriers to successful PRO implementation in RW studies. Their work pioneered the identification of critical requirements for RW-PRO use, emphasising the need for primary research characterised by robust scientific methodology within this field.

The topicality of issues around the utilisation of RW-PROs was confirmed by the ISPOR COA Special Interest Group (SIG) work. The SIG attempted to enhance understanding of the challenges of using COAs, including PROs, in RW studies. The SIG conducted the ISPOR-wide survey in November 2019 to identify:

- best practices for the design, use, and analysis of COA data in RW studies;
- methods for operationalisation of COAs in RW studies, and
- regulatory guidance for the use of COAs in RW studies.

The survey was followed by roundtable discussions attended by international experts representing the FDA, EMA, CADTH, and pharmaceutical industry. The panel discussed the challenges in implementing COAs into RW studies.[147] The identified concerns included:

- lack of transparency about study design in RW studies;
- analysis of COA data in RW studies, specifically a lack of a priori planning;
- missing data mitigation;

- current guidelines (RWE-specific and COA-specific) do not sufficiently cover the use of COAs in the RW context.[147]

The above-mentioned works have shown a growing interest in collecting PROs in the RW setting. It is parallel to the increase in the use of RWE to inform various decisions being made in the healthcare space.[110] Multiple stakeholders acknowledged the potential of RW-PROs and the existence of numerous barriers hampering their successful implementation.[146, 147] To what extent these hopes will materialise and how to incorporate RW-PRO to advance healthcare research remains unclear. Methodologically robust studies were needed to deepen issues initially explored by Calvert et al. and SIG work. These include the availability of guidance supporting the use of RW-PROs, stakeholders' perspectives on barriers hampering their full implementation and opportunities associated with their adoption. Thus, this PhD project aimed to help answer some of these questions using robust scientific methodology.

1.4 Aims

This thesis aimed to describe PRO utilisation patterns in RWE generation and identify challenges and opportunities for successfully implementing RW-PROs.

1.5 Objectives

The overall aims of the thesis were reached by meeting the following objectives:

1) To identify and summarise existing guidance for using PROs in RWE generation.
2) To quantify and describe utilisation patterns of PROs in RW studies.
3) To explore in-depth perspectives of international stakeholders about challenges and opportunities for using RW-PROs.
4) To identify strategies enhancing the uptake of PROs in the RWE generation.

1.6 Structure

The thesis consists of separate studies to address the objectives detailed above:

- Chapter 3 contains a systematic review of guidance for collecting and using PROs in RWE generation – published in the Journal of Patient-Reported Outcomes in 2022. This addresses objective 1.
- Chapter 4 presents the results of the quantitative analysis of the ClinicalTrials.gov database to identify RW studies capturing PROs – published in the Contemporary Clinical Trials in 2022. This addresses objective 2.
- Chapter 5 presents a qualitative study of interviews with international stakeholders to explore their views on the current and future use of PROs in RWE generation – published in Heliyon in 2023. This addresses objectives 2, 3 and 4.

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Chapter 2: Methods

2.1 Introduction

This chapter provides an overview of the methodology adopted to address the aims and objectives of this research. It also justifies the methods selected and discusses alternative approaches that were considered. In-depth information about the methods used is provided in corresponding chapters (Chapters 3-5) and appendices.

A mixed-methods approach, which integrates qualitative and quantitative research elements, was selected as the most suitable methodology for this PhD research.[1] This approach addresses the research objectives, such as describing PRO utilisation patterns in RWE generation and identifying challenges and opportunities for the successful implementation of RW-PROs. By integrating both quantitative and qualitative methods, the study offers a comprehensive response to the complex aspects of the research question, leveraging the strengths of each method to enhance the understanding of the subject.[2]

Furthermore, findings from earlier phases of this research informed the design of subsequent phases. For instance, key recommendation categories identified in the SLR (Chapter 3) guided the selection of the qualitative framework for data analysis in interviews (Chapter 5). Additionally, insights from the SLR related to the current availability of RW-PRO guidance shaped the development of interview topic guides (Chapter 5) and contributed to hypotheses about the lower utilisation of PROs in phase IV trials, as discussed in Chapter 4.

In this study, qualitative and quantitative elements were used complementarily to enrich the interpretation of findings and provide more robust answers to the research question, distinguishing it from a multi-methods approach. Unlike mixed-methods research, multi-methods research employs various methods independently to address different aspects of the research question without integrating them within a single study.[3, 4] Table 2.1 illustrates the mixed-methods research process adopted throughout this PhD project.

Table 2.1. Mixed-methods research process.

<table>
<tr><th>Chapter</th><th>Knowledge gaps</th><th>Objectives</th><th>Methods</th></tr>
<tr><td>3</td><td>Need to understand what guidance on PROs in RWE generation exist</td><td>To identify and summarise existing guidance for using PROs in RWE generation</td><td>A systematic review of guidance for collecting and using PROs in RWE generation</td></tr>
<tr><td>4</td><td rowspan="2">Uncertainty about how often RW studies utilise PROs</td><td rowspan="2">To quantify and describe utilisation patterns of PROs in RW studies.</td><td>Quantitative analysis of the ClinicalTrials.gov database to identify RW studies capturing PROs</td></tr>
<tr><td rowspan="3">5</td><td rowspan="3">Qualitative interviews with international stakeholders to explore their views on the current and future use of PROs in RWE generation</td></tr>
<tr><td>Important barriers and facilitators for RW-PRO use are unknown</td><td>To explore in-depth perspectives of international stakeholders about challenges and opportunities for using RW-PROs</td></tr>
<tr><td>Need to identify strategies allowing to fully benefit from the inclusion of PROs in RW studies</td><td>To identify the most promising strategies to enhance the uptake of PROs in the RWE generation</td></tr>
</table>

2.2 Systematic review

2.2.1 Overview

To address objective 1 of this doctoral research – identify all available guidance for using PROs in RWE generation - systematic review was chosen as an appropriate method of information synthesis. Identifying all relevant publications and minimising the risk of missing key documents was paramount. Detailed information about the methodology followed in conducting the systematic review is presented in Chapter 3. This section justifies the selection of this particular method and discusses alternative ways of information synthesis.

2.2.2 Justification for choice of methods

Systematic reviewes provide a thorough and objective overview of existing information on a specific topic. They are considered the highest quality evidence aggregation methods in hierarchies of research evidence and are commonly used in health technology assessment under the paradigm of evidence-based medicine.[5] Well-designed and robustly executed systematic reviewes may provide comprehensive, unbiased, and credible evidence on the research question of interest. They follow a rigorous methodology, which should be specified before conducting the searches. Reviewers must carefully record and transparently report all steps undertaken. Systematic reviews are widely accepted methods for evidence synthesis by various healthcare decision-makers.[6] They are commonly used to inform practice guidelines development and policy decision-making. Carefully reported methods and decisions made as part of the

systematic review process allow for replication of work by other researchers, enhancing transparency and reliability.[7]

As one of the priorities for the research presented in Chapter 3 was to identify all relevant studies and produce a comprehensive overview of available guidance, systematic review was deemed the appropriate method to follow. Moreover, a pre-defined search strategy, *a priori* inclusion and exclusion criteria, and two independent reviewers were used to minimise bias.

Several resources providing advice on performing systematic reviews are available. Cochrane Collaboration provides guidelines for preparing and maintaining systematic reviews of the effects of health interventions.[8] Moreover, Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) cover a widely accepted standard for reporting systematic review results.[9] A PRISMA checklist was completed for the review presented in this thesis and can be found in Appendix 3.1.

Registering protocols of systematic reviews in the International Prospective Register of Systematic Reviews (PROSPERO) is a good practice.[10] This procedure was also followed in the case of the review presented in Chapter 3. Systematic reviews are a resource-intensive, costly and time-consuming mode of information synthesis. Researchers are urged to conduct a search of the PROSPERO database prior to commencing systematic reviews to check that similar reviews are not already underway. Pre-registration therefore prevents duplication of work by different research groups. It also promotes accountability as reviewers are obliged to follow pre-specified protocols, encompassing inclusion and exclusion criteria, preventing them from modifying these

parameters in due course without providing valid justification. The PROSPERO register was searched, and no comparable review, to the one presented in this thesis, was identified.

2.2.3 Alternative methods

Several different types of reviews can be used for evidence synthesis. The review article by Grant and Booth[11] reported 14 different kinds of reviews and provided their descriptions. This section will mainly focus on two alternative types of review: critical review and rapid review.

A critical review aims to identify the most important publications in a field. There are no formal quality assessment criteria for this type of work. Usually, narrative synthesis is followed to present the output. This type of review is more vulnerable to bias, as the reviewer's views and opinions can significantly impact the selection of the relevant publications and data extraction. On the other hand, these characteristics can be seen as an advantage when approaching some research questions, especially when an interpretation of previous research in the field is desired.[11]

On the other hand, rapid review represents the steps followed in the systematic review process. Although, the completeness of the search is determined by time and resource constraints. In other words, it is a simplified version of a systematic review, usually with limited data sources being investigated.[11]

It was decided to follow the systematic review method in this doctoral research. The output's completeness and robustness were crucial, and a systematic review was considered the appropriate method that could meet these requirements.

2.3 Quantitative analysis of ClinicalTrials.gov

2.3.1 Overview

Research presented in Chapter 4 aimed to quantify the utilisation of PROMs in RW studies (objective 2 of the thesis). Previous examples of research investigating the level of incorporation of PROs into clinical trials were identified.[12, 13] These studies scrutinised the ClinicalTrials.gov database[14] but did not restrict their searches to RW studies.

2.3.2 Justification for choice of methods and alternative approaches

2.3.2.1 Selection of database under investigation

The first consideration was the choice of database to be searched. Clinical study sponsors are required to register interventional trials in the public domain before the commencement of the study. Multiple clinical trial registries exist in different jurisdictions. The World Health Organisation’s (WHO) International Clinical Trials Registry Platform (ICTRP)[15] is an internet portal which aggregates records of clinical trials contained in local registries. Utilising this database would enable the most comprehensive geographic coverage of the review. Unfortunately, after scrutinising the ICTRP database snapshot, it was realised that it contains many missing data about the clinical trial phase. Thus, it would have been impossible to easily identify RW studies using this database.

Finally, it was decided to focus on the ClinicalTrials.gov database. ClinicalTrials.gov is the largest and well-known register of clinical trials. It is run by the US government but covers trials conducted globally. Moreover, ClinicalTrials.gov provides extensive descriptions of various trials' characteristics.

2.3.2.2 Selection of the review method

Another consideration was the choice of a technique to identify the studies that collect PROMs to assess health outcomes. Manual screening (similar to systematic review of literature) and automated computer algorithms were considered.

Substantial variation existed in the manner in which the trials retrieved from the ClincalTrial.gov database specified the PROs intended for collection, e.g., by providing PROM's full name, abbreviated name, umbrella terms like QoL, or simply by mentioning "PRO" in the trial description. Given the variation in how PROs were described, manual screening would have carried a lower risk of omission of relevant trials.

Whilst human selection of relevant studies can be considered a gold standard, manual review is labour-intensive and time-consuming. The ClinicalTrial.gov database held almost 30,000 records of phase IV trials at the time of this research (July 2021). It was not feasible to manually screen all these records in a reasonable time frame. Given the impracticalities of conducting a manual screening of all the potentially relevant entries, an option was to manually screen a subset of ClinicalTrials.gov records focusing on the most recently registered trials. The alternative was to use a computer algorithm that could flag relevant studies since the database's inception. Finally, it was decided that the breadth of

the review is favourable. Thus, similarly to previously published studies [12, 13], an automated algorithm was chosen as an appropriate technique.

2.3.2.3 Brief description of the automated algorithm utilised

After reviewing previously published papers, it was decided that the quantitative analysis presented in this thesis will build on the work of Vodicka et al.[12]. Nevertheless, the algorithm used to search the ClinicalTrials.gov database snapshot was developed *de novo* as part of this research project. Data compilation and processing were done in Python v.3.8.8. Alternative methods for matching search terms against trial characteristics considered are presented in Table 2.2.

Table 2.2. Matching methods for trial identification.

Nr	Method	Description
1	Exact match	Simple searching of a text string
2	Fuzzy string matching algorithm[16]	Matches the sentences using Levenshtein Distance[17]
3	Word ratio	Calculates the ratio of words that are similar between the compared terms
4	Word2vec[18]	Counts words for each term into vector
5	TF-IDF[19]	Counts words for each term into a vector, but the most important words are assigned with greater weight

A sample of records was manually screened to validate the accuracy of alternative matching techniques. After comparing the algorithms' validation parameters, the "exact matching" method was chosen. It proved to have the highest accuracy of all the compared approaches. The algorithm settings covering techniques for text transformation, length of

compared text strings and inclusion of various fields to be searched were iteratively revised to maximise accuracy.

Similar to Vodicka et al.[8], the Patient-Reported Outcomes and Quality of Life Instruments Database (PROQOLID)[20] was used to construct the search term list. Apart from full and abbreviated PROM names contained in PROQOLID, umbrella terms describing PROMs and quality of life measures were added to that list. It was necessary as clinical trial descriptions available on ClinicaTrials.gov used various phrases when referring to collected PROMs. Some referred precisely to PROMs names, while others mentioned general terms like: “HRQoL” or “PRO”.

“Phase IV trials” and “RWE” are not interchangeable terms. RWE is a broader concept and usually relates to the totality of evidence generated in post-marketing studies to inform regulators and payers to improve patient access to safe and effective treatments. Further considerations around the definition of RWE are presented in section 1.2.9. Phase IV studies represent only one type of RW study. They were used as a proxy to illustrate the utilisation of PROs in RWE generation. The main reason for this simplification was the ease with which phase IV trials can be distinguished in the ClinicalTrials.gov database. Incorporating different definitions of RW study would be cumbersome and could lead to misclassifying some studies. Although our analysis was restricted to phase IV clinical trials, it is deemed a reasonable indication of PRO utilisation in the RWE space.

Overall, the quantitative analysis presented in this thesis updated previously conducted searches using the same database and restricted inclusion criteria to phase IV studies only.[12] A *de novo* automated algorithm allows for the reproducibility of results and

analysis of extensive datasets. The algorithm's satisfying performance was proven by comparing its output with a manually screened sample.

2.4 Stakeholder interviews

2.4.1 Overview

Qualitative one-to-one interviews with international stakeholders are chosen as an appropriate method to address objectives 3 to 5 of this doctoral research. They enable the deeper exploration of participants' perspectives on the current and future use of PROs in the RWE generation and identify challenges and opportunities for RW-PROs' use. One-to-one semi-structured interviews also allow to elicit possible strategies for the successful implementation of PROs in the RWE generation. This section justifies method selection and describes the research process.

2.4.2 Ethical approval

As the study presented in Chapter 5 recruited human participants, the review by the ethical committee was necessary before the commencement of the fieldwork. According to the University of Birmingham Code of Practice for Research[21], the Science, Technology, Engineering and Mathematics Ethical Review Committee approved this research under the reference number ERN_21-1240. The Committee has also reviewed relevant study materials, including:

- Patient experts' consent form – Appendix 2.1;
- Other experts' consent form – Appendix 2.2;
- Patient experts' participant information sheet – Appendix 2.3;

- Other experts' participant information sheet – Appendix 2.4;
- Patient experts' interview topic guide – Appendix 5.1;
- Other experts' interview topic guide –Appendix 5.2.

2.4.3 Justification for choice of methods and alternative approaches

2.4.3.1 Qualitative research methods

Quantitative research methods aim to describe the size of the phenomena, compare and describe relationships between them.[22] In contrast, qualitative methods aim to reveal mechanisms and motivations causing observed behaviours or experiences.[23] The latter was of interest to address research objectives 3-5 of the thesis. Thus, qualitative methodology was used to explore stakeholder perspectives on the use of PROs in RWE, the results of which are presented in Chapter 5. Larger quantities of rich and detailed information from one-to-one interviews allow to understand participants' views better.[23]

The research question focuses on better understanding participants' experiences, perspectives, and attitudes towards RW-PROs. Qualitative methods allow for in-depth exploration, which would not be possible to capture by utilising quantitative methods. RW-PRO implementation is a complex issue with multifaceted potential consequences for various healthcare system actors. Qualitative research provides an opportunity to capture that complexity and reveal participants' views on this topic.[24] Moreover, qualitative research offers a unique opportunity to understand participants' lived experiences.[25] Patients' involvement was of paramount importance in answering research questions by illustrating their experiences and expectations associated with RW-PROs.

Last but not least, the study provided an excellent learning opportunity for the doctoral researcher due to its qualitative nature. Qualitative research methods are exploratory and allow to learn from the participants and adapt the interview schedule if needed. Apart from giving a chance to identify individuals' perspectives on the collection and use of PROs in the RW setting, it was also an opportunity to learn about the context of PRO use in routine care settings, applications of PROs in regulatory and reimbursement decision-making and contextualising it in the broader healthcare system context.

2.4.3.2 Interviews vs focus groups

One-to-one interviews allow for meaningful interactions with participants.[26] The individual nature of interviews makes it possible to capture the unique perspective of each participant.[26] That, in turn, facilitates deeper exploration of participants' opinions and should generate rich and nuanced data. It is easier to control the flow of a conversation and focus on relevant themes during the interview. This is usually much harder to attain during the focus group exercises – a common alternative to interviews.[27]

Focus groups collect views from a group of individuals. Focus groups can be helpful as they can benefit from the interaction between participants. The discussion dynamics between study subjects might generate concepts and ideas that would not be developed in isolation.[28] However, some participants can easily dominate focus groups, hampering the representation of all individuals' perspectives. Thus, a focus group might not be an adequate forum for modest participants.[29]

Thus, interviews were considered a more appropriate method at an early stage of the RW-PROs field. Moreover, the decision to pursue one-to-one interviews was a pragmatic one.

Organising a focus group would entail finding suitable dates for multiple stakeholders with busy schedules. As this study recruited international participants who live in different time zones, coordinating group meetings would add additional complexity.

2.4.3.3 Semi-structured interviews

A topic guide was used to direct the interviews. The topic guide was iteratively refined to improve the flow of the interview. Semi-structured interviews were chosen as an appropriate data collection technique. Semi-structured interviews can retain comparability between data gathered from different participants but allow for flexible reactions to the flow of a discussion and facilitate the collection of in-depth data.[24] Moreover, a semi-structured one-to-one interview allows a researcher to react to the participants' responses on an ongoing basis. Questions can be adapted to evolving situations. The flexibility of semi-structured interviews allows the capture of unexpected findings. Questions can be adjusted and deepen some of the essential aspects mentioned.

2.4.4 Framework selection

Theoretical frameworks are often used to guide the coding and analysis of data collected in qualitative studies. They are utilised to strengthen the robustness of study results. There are multiple theoretical frameworks available.[30] A targeted review of the most commonly used implementation frameworks for health research was undertaken to select an appropriate one for this study.

Seven implementation frameworks were identified, including:

- Consolidated Framework for Implementation Research (CFIR)[31];

- Sekhon’s Acceptability Framework (TFA)[32];
- Klein and Sorra's Innovation Implementation Model[33];
- Outcomes for Implementation Research[34];
- Theoretical Domains Framework (TDF)[35];
- Evidence-Based Practice Implementation in Public Service Sectors (EPIS)[36];
- Reach, Effectiveness, Adoption, Implementation, and Maintenance Model (RE-AIM Model)[37].

Descriptions of selected frameworks are presented in Table 2.3. Additionally, advantages and disadvantages for the context of use in this study were provided for each framework.

Table 2.3. Theoretical frameworks in health research.

Framework	Description	Advantages	Disadvantages
Consolidated Framework for Implementation Research (CFIR)	CFIR organises themes into the following categories (39 constructs organized into five domains): innovation, outer setting, inner setting, individuals, and implementation process “While considering the research question and evaluation objectives, each construct can be evaluated for its likelihood of: • being a potential barrier (or facilitator) to implementation; or • having sufficient variation across the	• Tailored to health interventions • Detailed – covers a broad range of topics related to: intervention, environment in which intervention will be implemented, organisation in which intervention will be implemented and implementation process • Widely used • Easy to adapt to diverse settings and scenarios • Available tools (e.g. interview guide tool, observation template, codebook template, NVivo project template, memo template, rating rules, meeting notes template, matrix template, strategy matching tool)	• Designed to assess potential barriers and facilitators to implementation in a closely defined setting (e.g., a particular organisation) • Themes might require adjustment to compose a tailored set of domains

	units of analysis (e.g., organizations)"	• Can be used for different types of evaluation (e.g. pre- and post-implementation) • CFIR does not need to be used to collect data; open data collection techniques can be utilised, and the CFIR can be used only for analysis	
Sekhon's Acceptability Framework (TFA)	A multi-construct theoretical framework can be applied to assess the acceptability of healthcare interventions from the perspective of intervention delivers and recipients Acceptability was defined as a multifaceted construct reflecting the extent to which people delivering or receiving a healthcare intervention consider it appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention The theoretical framework of acceptability (TFA) consists of seven component constructs: affective attitude, burden, perceived effectiveness, ethicality, intervention	• Tailored to health interventions • Distinction between prospective and retrospective acceptability • Suitable for both patients and HCPs • Available tools: quantitative (questionnaire items) and qualitative (topic guide) instruments for assessing the acceptability of complex interventions – applicable development and evaluation cycle • Universal to different settings	• Less detailed • Focuses solely on acceptability

	coherence, opportunity cost, and self-efficacy		
Klein and Sorra's innovation implementation model	Implementation effectiveness depends on the strength of an organization's climate for the implementation of that innovation and the fit of that innovation to targeted users' values Implementation outcomes: resistance, avoidance, compliance, commitment	N/A	• Developed not specifically for health interventions • Strong focus on innovation implementation within an organisation
Outcomes for Implementation Research	Implementation outcomes: Acceptability, adoption, appropriateness, feasibility, implementation cost, penetration, sustainability	• Tailored to health interventions • Suggested types of measurement for each outcome	• Less detailed
Theoretical Domains Framework (TDF)	TDF was initially developed for implementation research to identify influences on health professional behaviour related to the implementation of evidence-based recommendations Domains: knowledge, skills, social/professional role and identity, beliefs about capabilities, optimism, beliefs about consequences, intentions, goals,	• Tailored to HCPs' behaviours • Widely used	Focused solely on HCPs' attitudes and behaviours

	memory, environmental context and resources, social influences, emotion, and behavioural regulation		
Evidence-Based Practice Implementation in Public Service Sectors (EPIS)	Multi-level, four phase model of the implementation process, applicable to public sector services. Factors affecting implementation: • Outer context: sociopolitical, funding, client advocacy, interorganisational networks, intervention developers, leadership, public-academic collaboration • Inner context: organisational characteristics, leadership, individual adopter characteristics, innovation-value fit, fidelity monitoring/support, staffing	Differentiation between phases of implementation	Developed not specifically for health interventions
RE-AIM model	Model for evaluating public health interventions that assess five dimensions: • Reach • Efficacy • Adoption • Implementation • Maintenance	Tailored to health interventions	Less detailed

	These dimensions occur at multiple levels (e.g., individual, clinic or organization, community)		

Following the identification of relevant frameworks, three of them, which were considered the most appropriate, were subject to a mapping exercise. Recommendation categories identified in systematic review of guidance for the collection and use of PROs in RWE generation (Chapter 3) were matched against domains of the following three frameworks: CFIR, TFA, and RE-AIM. This exercise aimed to find the tangency points between frameworks and themes addressed by available guidance documents. It was believed that interview participants might mention issues similar to those presented in the guidance. Matrixes with record of matching exercise are available in Appendix 2.5.

The matching exercise revealed that the framework with the most similarities to available guidance is CFIR. The CFIR framework is a commonly used tool for characterising the determinants of effective implementation of innovations in healthcare.[38] The CFIR was chosen as the most appropriate theoretical framework for the purpose of this qualitative study.

2.4.5 Participants recruitment

A mixture of two approaches to participant recruitment was utilised: convenience and purposive sampling. Both of them are non-probability sampling methods.[39, 40] Convenience sampling selects participants for inclusion as they are the easiest for the

researcher to access. On the other hand, purposive sampling selects participants based on their characteristics desired in the study sample.[41]

Convenience sampling was used as most prospective participants were identified through the existing University of Birmingham Centre for Patient Reported Outcome Research's (CPROR) networks and contacts. Nevertheless, some were also identified as part of the systematic review presented in Chapter 3. On the other hand, purposive sampling was used to distinguish two groups of participants: patient experts (patients and patient advocates) and other experts (academic researchers, regulators, payers, and industry experts).

Patient experts were expected to have experience of living with chronic health conditions or advocating for chronically ill patients. PRO and RWE-specific knowledge was not required from patient experts. Relevant terms were explained in the study documentation, with an opportunity to ask questions in advance of the interview and at the beginning of each interview. Other experts were expected to have worked in the COA, RWE, or RCT space in various roles including regulatory, payer, research, or industry organisations, but again had opportunity to discuss any questions in advance as part of the consent process.

2.4.6 Data collection

Interviews were conducted until saturation was reached. This means no new information was discovered despite the additional interviews being conducted.[42, 43] Although there is a lack of transparency when justifying sample sizes in qualitative research, saturation in this study was reached when the researcher had not identified any new themes in three interviews.[44]

2.4.7 Data analysis

Deductive coding uses *a priori* selected framework comprising a number of themes for organising the collected data.[45] In contrast, the inductive approach lets the collected data guide the analysis process without a predetermined structure.[45]

Data gathered in this study were coded deductively according to the domains of the CFIR framework. Where appropriate, new sub-domains to the CFIR framework were created inductively to accommodate newly identified themes.

A triangulation exercise was carried out as part of the data analysis. Investigator triangulation is a strategy that involves using more than one researcher to analyse the same data.[46, 47] Preliminary findings were presented to a patient partner and industry expert. They reflected on the data gathered and discussed it with the researcher. Their observations and comments shaped the way study results are presented and interpreted. The main reason for using investigator triangulation is to increase the validity and reliability of research findings as well as to expand the perspectives of investigators involved in the study.[48] Further details on data collection and analysis are presented in Chapter 5.

2.4.8 Reflexivity

Applying reflexivity in qualitative research is recommended and involves reflecting on the effects of researchers' attitudes and previous experiences on what is being studied.[49] I (KM) was a primary investigator in this qualitative study. Although I have spent most of my professional life working in the area of health technology assessment and health economics, I have developed a deep interest in PRO research relatively recently. In my previous roles, including my involvement in the Polish HTA appraisal committee, I mainly

handled PROs as inputs for economics modelling or as results of RCTs investigating therapies under evaluation. Certainly, before commencing this research project, I had an opinion about the value of PRO data and their ability to inform reimbursement processes. I am aware that my personal views and previous experiences could influence how I conduct qualitative interviews or analyse collected data. To minimise the impact of the researcher's attitude on this study's results, several measures have been undertaken. First, while conducting the interviews, I strived not to reveal my opinion of the value of RW-PROs to the participants. I tried to create an opportunity for study participants for free expression of their thoughts on this topic. I avoided asking leading questions and tried to minimise my role to deepen the threads the participants mentioned. Additionally, the second researcher was involved in coding a random sample of interview transcripts. The involvement of a second person allows for greater objectiveness while analysing collected information. Moreover, I kept a log of my observations and ideas emerging during each interview. I reflected on this information throughout the study. When scrutinising information collected during interviews, I always tried to separate my beliefs and views from what could be actually observed among the gathered data.

2.5 Patient and public involvement and engagement

This PhD research project prioritised the incorporation of patient and public insights in its design, conduct and reporting. These efforts align with the University of Birmingham's commitment to fostering greater Public and Patient Involvement and Engagement (PPIE) in research.[50]

The definitions of involvement and engagement within the context of PPIE, as outlined by the National Institute for Health and Care Research (NIHR), will be presented to ensure clarity. Patient and public involvement refers to research conducted "with" or "by" the public, not simply "to", "about," or "for" them [51]. In contrast, engagement refers to activities focused on disseminating research findings to the public and patients.[52]

One patient partner actively participated throughout the project, from initial study design to manuscript reviews. His invaluable insights shaped the research direction and contributed to a robust scientific methodology.

Furthermore, another patient partner provided crucial feedback on the preliminary quantitative interview results presented in Chapter 5. The final data analysis reflected a richer understanding of the patient experience by integrating his perspective. Additionally, patients and patient advocates were recruited as research participants, further enriching the research with patient voices.

The research findings were disseminated through various channels to ensure accessibility to a broad audience. Peer-reviewed publications targeted academics, healthcare professionals and industry experts, while email newsletters, social media, and published interviews made the research accessible to the public. Additionally, presentations at conferences provided a platform to engage with a broad scientific audience. Patient representatives are increasingly attending such meetings. It poses an opportunity to directly reach patient communities with the research findings.

Patient representatives are also involved in ISPOR Task Force work, addressing the use of PROs in prospective real world studies, which can be seen as a follow-up of the research conducted as part of this PhD project.

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Chapter 3: Systematic review of guidance for the collection and use of patient reported outcomes in real world evidence generation to support regulation, reimbursement and health policy

3.1 Introduction

An understanding of existing guidance is an important first step for formulating optimal strategies for the implementation of PROs in RWE generation. Thus, one of the first steps of this doctoral research was to conduct a systematic review of available guidance.

This chapter addresses thesis objective 1: to identify and summarise existing guidance for using PROs in RWE generation. It was published in the Journal of Patient-Reported Outcomes (JPRO) (2nd June 2022) and is presented below in the journal format.

This article was recognised with **the 2023 ISOQOL Outstanding Article of the Year Award** for JPRO.

Appendices 3.1-3.3 contain the following systematic review supplementary materials:

- PRISMA 2020 checklist (Additional file 1)
- Search strategy (Additional file 2)
- Data extraction (Additional file 3)

The work has been further disseminated as outlined in Table 3.1.

Table 3.1. Dissemination of publication 1.

Nr	Year	Conference/Publication	Type of communication
1	2023	ISOQOL 30th Annual Conference: Industry SIG symposium (Calgary)[1]	Oral presentation
2	2023	20th Global Cardiovascular Clinical Trialists Forum (Washington DC)[2]	Oral presentation
3	2024	ISOQOL QualityTALK newsletter[3]	Editorial

3.2 References

1. *30th Annual Conference of the International Society for Quality of Life Research.* Quality of Life Research, 2023. **32**(2): p. 23-220.
2. CVCT Forum. *CVCT Scientific Program 2023*. 2023; Available from: https://www.globalcvctforum.com/scientific-program-2023.
3. Maruszczyk, K., et al. *How much do we know about using patient-reported outcomes for real world evidence generation?* ISOQOL QualityTALK 2024; Available from: https://www.isoqol.org/using-pros-for-rwe-generation/.

3.3 Publication 1

Konrad Maruszczyk, Olalekan Lee Aiyegbusi, Barbara Torlinska, Philip Collis, Thomas Keeley, Melanie J Calvert. Systematic review of guidance for the collection and use of patient-reported outcomes in real-world evidence generation to support regulation, reimbursement and health policy. Journal of Patient-Reported Outcomes, 2022. 6(1): p. 57. https://doi.org/10.1186/s41687-022-00466-7

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Journal of Patient-Reported Outcomes

REVIEW Open Access

Systematic review of guidance for the collection and use of patient-reported outcomes in real-world evidence generation to support regulation, reimbursement and health policy

Konrad Maruszczyk[1,2], Olalekan Lee Aiyegbusi[1,2,3,4,5], Barbara Torlinska[1,2,3], Philip Collis[1,5], Thomas Keeley[1,6] and Melanie J. Calvert[1,2,3,4,5*]

Abstract

Background: Real-world evidence (RWE) plays an increasingly important role within global regulatory and reimbursement processes. RWE generation can be enhanced by the collection and use of patient-reported outcomes (PROs), which can provide valuable information on the effectiveness, safety, and tolerability of health interventions from the patient perspective. This systematic review aims to examine and summarise the available PRO-specific recommendations and guidance for RWE generation.

Methods and findings: Medical Literature Analysis and Retrieval System Online, Excerpta Medica Database, and websites of selected organisations were systematically searched to identify relevant publications. 1,249 articles were screened of which 7 papers met the eligibility criteria and were included in the review. The included publications provided PRO-specific recommendations to facilitate the use of PROs for RWE generation and these were extracted and grouped into eight major categories. These included: (1) instrument selection, (2) participation and engagement, (3) burden to health care professionals and patients, (4) stakeholder collaboration, (5) education and training, (6) PRO implementation process, (7) data collection and management, and (8) data analysis and presentation of results. The main limitation of the study was the potential exclusion of relevant publications, due to poor indexing of the databases and websites searched.

Conclusions: PROs may provide valuable and crucial patient input in RWE generation. Whilst valuable insights can be gained from guidance for use of PROs in clinical care, there is a lack of international guidance specific to RWE generation in the context of use for regulatory decision-making, reimbursement, and health policy. Clear and appropriate evidence-based guidance is required to maximise the potential benefits of implementing PROs for RWE generation. Unique aspects between PRO guidance for clinical care and other purposes should be differentiated. The needs of

Philip Collis: Patient partner

*Correspondence: m.calvert@bham.ac.uk

[1] Centre for Patient Reported Outcome Research, Institute of Applied Health Research, University of Birmingham, Birmingham, UK
Full list of author information is available at the end of the article

various stakeholder groups (including patients, health care professionals, regulators, payers, and industry) should be considered when developing future guidelines.

Keywords: PRO, RWE, Patient-reported outcomes, Real-world evidence, Guidelines, Recommendations

Introduction

Real-World Evidence (RWE) is defined by the U.S. Food and Drug Administration (FDA) as clinical evidence assessing benefits and risks of a medical product derived from analysis of real-world data (RWD) [1]. RWE can be generated prospectively and retrospectively by different study designs [1]. RWD in turn is defined as "data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources" [1]. The most common RWD sources are: electronic health records, claims databases, registries, and patient-generated data [1].

Currently, there is increasing recognition from global regulators, payers, and policy makers that patient-reported outcomes (PROs) — reports of health status directly provided by patients, without interpretation by a clinician or anyone else [2] — can provide valuable information on effectiveness, safety and tolerability from the patient perspective [3–6]. The U.S. FDA's framework for Real-World Evidence Program acknowledged that PROs provide unique and valuable information which may complement the evidence obtained using traditional clinician-focused parameters [7]. The agency recently published its RWD draft guidelines on data sources, data standards, and regulatory considerations [8–11]. However, these guidelines make limited reference to PROs beyond referencing existing FDA 2009 guidance [12] and ensuring appropriate monitoring of the study, including where applicable, PROs.

It is also worth noting that PROs constitute a key part of U.S. Centers for Medicare & Medicaid Services Meaningful Measures Framework [13]. In the UK, the Medicines & Healthcare products Regulatory Agency (MHRA) recently issued two guideline documents focusing on the use of RWD to support regulatory decisions [14, 15]. The European Medicines Agency (EMA) currently uses RWE for safety monitoring and recently announced that the use of RWE will be established across its spectrum of regulatory use cases by 2025 [16].

Moreover, the recognition of the importance of PROs has led to a growing interest and increase in sponsorship by the pharmaceutical industry of real-world long-term safety studies which incorporate the longitudinal collection of PROs. Currently the PRO data for RWE generation are collected mainly in post-authorisation studies to support labelling claims, reimbursement and health policy making. For instance, the post-authorisation efficacy study for mepolizumab in the treatment of severe asthma [17] and post-authorisation efficacy and safety study for fingolimod in patients with relapsing–remitting multiple sclerosis [18] showed that the effectiveness of the drugs is consistent with clinical trial results under real-world settings.

In real-world contexts, prospective PRO collection has been limited and fragmented, with PROs collected in only 14% (8 out of 57) of recent post-authorization safety studies, consisting largely of one-off registries for post-marketing assessment sponsored by drug manufacturers in specific populations [19]. However, increasing collection of PROs in routine clinical care to support individual decision making and audit/benchmarking offers emerging opportunities to use the PRO data for multiple purposes including the assessment of real-world efficacy, safety, and tolerability of health interventions for regulatory, reimbursement and health policy purposes.

Several guidelines on the implementation of PROs exist but mainly focus on RCTs or clinical practice [5, 12, 20–25] and provide little or no recommendations for the use of PROs in the context of RWE generation, addressing the needs of regulators and policy makers. Therefore, the aim of this systematic review was to examine relevant literature and summarise PRO-specific recommendations for RWE generation to support regulation, reimbursement, and health policy, and highlight areas for future research.

Methods

Scope of the review

The review focused on PRO-specific recommendations for RWE generation. PROs were differentiated from other types of patient-reported or generated data, such as PREMs, unstructured patient-generated health data, patient-reported data about medication used, health care utilisation or events.

Studies were included if they provide recommendations for the use of PROs in RWE generation to support regulation, reimbursement, and health policy. No date limits or country restrictions were applied. In order to capture all available recommendations for PRO use in RWE generation, eligibility was not restricted to formally issued guidelines but also included any publications with recommendations or opinions on PROs in RWE generation including research, reports, discussion papers, books, commentary/opinion pieces and editorials.

Publications containing broad recommendations for PRO use only, e.g., general statements supporting PRO data collection in real-world setting or indicating the usefulness of PRO data, or highlighting the need for more patient-centric RWE research [8–11, 14–16, 26–29] were excluded. However, these were referenced in our discussions where appropriate.

Publications providing recommendations solely on the use of PROs in RCTs or to guide clinical care, and clinical RWE studies were excluded [23, 24, 30].

Search strategy and publication selection

The systematic review was conducted according to a protocol registered in International Prospective Register of Systematic Reviews (PROSPERO), registration number: CRD42021235709. It was reported in compliance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [31] (see Additional file 1 for the completed PRISMA checklist). Medical Literature Analysis and Retrieval System Online (MEDLINE) and Excerpta Medica Database (EMBASE) were searched using broad search terms to identify relevant publications. The search was conducted using the controlled vocabulary and free text of the relevant databases. These included words related to "real-world evidence", "patient-reported outcomes", "guidelines" and "recommendations". Moreover, the search terms used were adapted from published database search filters for "quality of life" [32] and "guidelines" [33]. No language or publication date restrictions were applied. For the full search strategy, see Additional file 2. Database searches were conducted on January 18, 2021. Two reviewers (KM, BT) independently screened the titles and abstracts according to the inclusion and exclusion criteria. Following this, the reviewers independently assessed the full texts of potentially relevant studies. At each stage, disagreements were resolved by discussion between the reviewers. If no consensus were reached, senior project members were consulted (MC, OLA). Records of screened entries, along with the reviewers' reasons for inclusion and exclusion were held in EndNote X9 referencing software. When relevant conference abstracts were identified, we attempted to identify the full-text publication or conference output.

Other potentially relevant publications were identified from forward and backward citation searching of included studies. In addition, the grey literature was searched using a combination of the search terms from the original database search. Sources were:

- Google Scholar (100 first hits);
- HTA (Health Technology Assessment) agency websites: Canadian Agency for Drugs & Technologies in Health (CADTH), Haute Autorité de santé (HAS), The National Institute for Health and Care Excellence (NICE) and International HTA database, and NHS Evidence;
- Regulator websites: EMA and FDA;
- Professional organisations: Society for Health Economics and Outcomes Research (ISPOR), International Society for Quality of Life Research (ISOQOL), Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints (SISAQoL) Consortium, Patient-Centered Outcomes Research Institute (PCORI), Agency for Healthcare Research and Quality (AHRQ), and International Society of Pharmacovigilance (ISOP).

Data extraction

Relevant data were extracted into an Excel spreadsheet from the included publications by one reviewer (KM) and checked for accuracy (by BT). Data related to the following areas were extracted wherever possible: guidance issuing body, aim of the guidance, clinical area, patient population and recommended PRO instruments. Moreover, domains, described in the paper by Calvert et al. [6], were used as an initial framework for data extraction covering: objectives; patient population; instrument selection; frequency of administration; mode of administration; data collection method; data monitoring; presentation of results; ethics; data ownership and consent; audit; privacy; feedback to clinicians, patients, healthcare providers, drug manufacturers, regulatory authorities; and resources needed. Additional categories were added if identified information did not match any of the previously described domains. All extracted PRO-related recommendations were re-arranged into a smaller number of categories around similar issues addressed by the publications. Finally, these domains were grouped into major categories.

Results

Study selection

The search strategy identified 1,453 potentially eligible entries, of which 1,249 remained after removing duplicates. After screening titles and abstracts, 1,198 entries were excluded, leaving 51 publications for full-text screening. Of these, five met the study inclusion criteria. An additional two entries were identified by reference and website searching, resulting in a total of seven publications included in the review. The PRISMA flow diagram (Fig. 1) provides an overview of the review process and study selection.

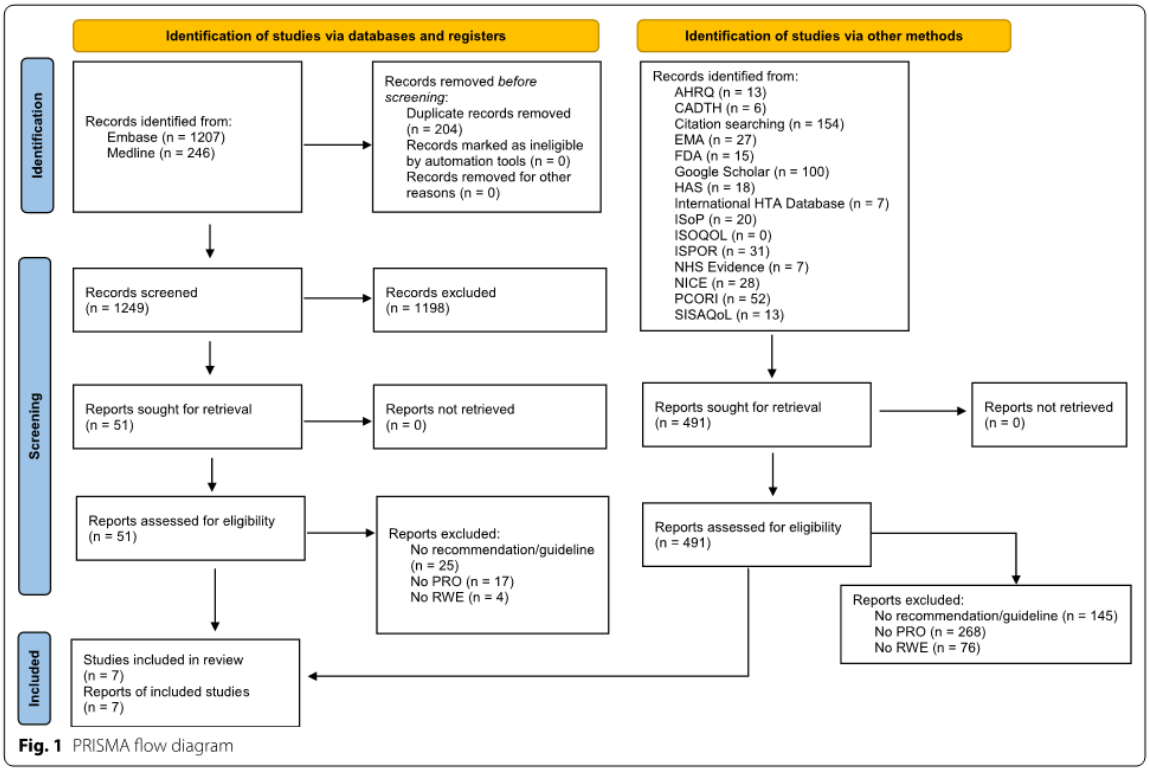

Fig. 1 PRISMA flow diagram

Characteristics of included publications

The summary characteristics of all seven publications are presented in Table 1. Four were published in peer-reviewed journals [6, 34–36], two were conference posters [37, 38] and one was an online published report [39]. Four of the publications [6, 36, 37, 39] did not focus on a specific patient population or clinical area and provided recommendations applicable to the general patient cohorts. One of the publications focused on patients with dementia [34] and one gave recommendations focused on elderly patients [38]. One paper discussed PRO data collection among patients undergoing selected surgical interventions [35].

The included publications provided recommendations for PRO data collection and its use in different RWE settings. Two papers gave general recommendations relevant to real-world research [37, 39]. The remaining publications focused on: drug development [6], post-authorisation safety evaluation [35, 36, 38] and pragmatic clinical trials [34].

Recommendations issued

The recommendations provided were grouped into eight major categories: (1) instrument selection, (2) participation and engagement, (3) burden to health care professionals (HCPs) and patients, (4) stakeholder collaboration, (5) education and training, (6) PRO implementation process, (7) data collection and management, and (8) data analysis and presentation of results.

An overview of the recommendation categories is presented in Table 2. Additionally, detailed data extracted from included studies for the major categories can be found in Additional file 3.

Instrument selection

Five of seven included publications provided some level of advice about choosing appropriate PRO measure [6, 34–37]. PRO measure selection was discussed in the context of: instrument suitability for the target population, availability of relevant psychometric evidence supporting the use of PRO instrument in a given context and adaptation of existing instruments or development of new measures.

Calvert et al. [6] gave a broad recommendation stating that PROs measures used in the RWE setting need to be valid, consistent with the intended use and relevant to the identified needs of the target population. Banerjee et al. [36] proposed a core minimum dataset (including PROs)

Table 1 Characteristics of individual studies

Author	Year	Issuer	Publication type	Patient population	Context for PRO usage	Aim of the publication	Scope of the publication
Hanson et al. [34]	2020	Division of Geriatric Medicine, University of North Carolina	Journal article	People with Dementia	Pragmatic Clinical Trials	To promote optimal use of outcomes relevant to people leaving with dementia and their caregivers in pragmatic trials	PCRO Core was proposed to promote optimal use of outcomes relevant to PLWD and their caregivers in pragmatic trials
Calvert et al. [6]	2019	CPROR, University of Birmingham	Comment	General	Drug development	To describe key challenges for use of PROs as part of RWE by payers and regulators	Overview of challenges in collecting, analysing, and integrating PRO data with other forms of RWE. Putting forward strategic priorities to help address these challenges
Rylands et al. [37]	2018	pH Associates (an OPEN Health company)	Conference poster	General	Research (various designs using RWD)	To summarise the key considerations for researchers collecting PRO data in RW studies	Summary of the key considerations for PRO data collection. Authors postulate the creation of a specific set of guidelines
Kyte et al. [35]	2016	CPROR, University of Birmingham	Journal article	Patients undergoing varicose vein, groin hernia and hip replacement surgery	Post-authorisation safety studies	To evaluate NHS PROMs programme for routine PRO data collection	Pointing areas for improvement in routinely collected PROs within NHS
Akiyama et al. [38]	2015	Bayer Yakuhin, Ltd	Conference poster	Elderly patients	Post-authorisation safety studies	To describe challenges and propose best practices for conducting post-marketing surveillance PRO surveys among elderly patients	A brief overview of challenges in collecting and using PRO data from elderly patients as part of post-marketing surveillance. Proposing best practices to help address these challenges
Banerjee et al. [36]	2013	PROSPER Consortium	Journal article	General	Safety reporting	To develop guidance on PRO-AE data, including the benefits of wider use and approaches for data capture and analysis. To support the wider use of PROs in safety reporting (pharmacovigilance)	Providing PRO-AEs taxonomy, suggesting a range of datasets that could be used for safety reporting, data collection mechanisms and analytical methodologies. Minimum core dataset for use by industry or regulators to structure PRO-AEs was proposed
ABPI [39]	2011	ABPI	Report	General	Research (various designs using RWD)	To provide further clarity around the definitions, use and practical issues which arise when undertaking RWD projects	Presentation of terminology related to RW studies. Methodological recommendations for RWD generation to be used for research, audit, and service evaluation purposes

ABPI The Association of the British Pharmaceutical Industry; *CPROR* Centre for Patient Reported Outcome Research; *NHS* National Health Service; *PCRO* patient- and caregiver-reported outcomes; *PLWD* people living with dementia; *PRO* patient-reported outcome; *PROM* patient-reported outcome measure; *RW* real-world; *RWD* real-world data; *RWE* real-world evidence

Table 2 Overview of recommendations categories

Recommendation categories	Hanson et al. [34]	Calvert et al. [6]	Rylands et al. [37]	Kyte et al. [35]	Akiyama et al. [38]	Banerjee et al. [36]	ABPI [39]
Measure selection	●	●	●	●	○	●	○
Participation and engagement	●	●	●	●	●	○	●
Burden to HCPs and patients	●	●	●	○	○	○	○
Stakeholder collaboration	○	●	○	○	○	○	○
Education and training	●	○	○	●	●	○	○
PRO implementation process	○	●	○	●	●	●	●
Data collection and management	●	●	●	●	●	●	●
Data analysis and presentation of results	○	●	○	●	○	●	●

● Includes, ○ Does not include.

for non-regulated consumer websites listing information which should be collected from patients to allow for post-approval safety monitoring. Hanson et al. [34] highlighted the need for outcome measures to address patient or caregiver-centred outcome domains and to be acceptable to respondents.

The need for a definitive evidence base for PRO measures selected for use in a clinical setting was emphasized by Kyte et al. [35]. Hanson et al. [34] suggested that measure attributes such as psychometric properties (e.g. validity, reliability, sensitivity to change, floor/ceiling effect) should be considered when selecting PRO measures to identify instrument fit for purpose.

For situations where no appropriate measures are available, Hanson et al. [34] suggested the adaptation of existing measures or the development of de novo instruments. Particular attention was given to translation of existing questionnaires. Despite not recommending specific measures, authors often underlined the importance of using well translated PRO measures. Hanson et al. [34], Rylands et al. [37] and Calvert et al. [6] stressed the importance of adaptation and translation of PRO measures to ensure they match the literacy skills and are culturally relevant to diverse patient populations.

Participation and engagement

This category was split in two sub-domains. The first focuses on recommendations aiming to improve patient participation in a study and enhance quality of collected data. The second focuses on the involvement of different stakeholders in study design or conduct.

Study participation Authors of four publications [6, 34, 37, 38] gave recommendations to strengthen patient participation in RWE studies. Calvert et al. [6] recommended to make questionnaires available in different languages to meet language requirements of diverse patient populations. Hanson et al. [34] stated that outcome measures used, should address patient or caregiver-centred outcome domain and be acceptable to respondents. Rylands et al. [37] noted that patient engagement and mode of recruitment strongly depend on the level of patient contact with healthcare services. Thus, it would be beneficial to consider the frequency of clinic visits required by patients when designing a study using RWD. Akiyama et al. [38] postulated that special attention is required at the participating sites for elderly patients. For example, large letters and simple wording may be helpful to be used for explanatory document and questionnaires dedicated for elderly patients. Also, posters and flyers may be used to promote the study.

Study development and conduct Stakeholder involvement in designing RWE studies was recommended by five studies [6, 34, 35, 38, 39]. Greater HCP and health care providers involvement in planning study and data collection activities is beneficial. Akiyama et al. [38] noted the importance of involving clinicians with keen interest in PROs as it is key for successful data collection. Greater involvement of external stakeholders (payers, regulators, industry) in RWE studies can be obtained by demonstrating its benefits and importance to these organisations [34].

Hanson et al. [34] and Akiyama et al. [38] suggested to engage stakeholders early, particularly during PRO measure development process. Hanson et al. [34] focused mainly on collaboration with key stakeholders such as health system leadership. On the other hand, Akiyama et al. [38] and the ABPI [39] focused on both collaboration between internal (within industry or RWE study team) and external stakeholders (external experts, payers, regulators). Informing both internal and external stakeholders about justifications for PRO data collection for RWE and communicating to them the value of PRO assessments was also recommended [34, 38, 39].

Three publications stressed the importance of stakeholder involvement in PRO measure selection [6, 35, 38].

Focus groups and pilot tests were proposed as methods for enhancing stakeholder's participation in measure selection or development.

Burden to HCPs and patients

The importance of not overburdening patients, clinicians and health care providers with frequent and lengthy data collections were described as key to the successful implementation of PRO measures for RWE generation. Hanson et al. [34] mentioned that paper questionnaires or patient interviews typically impose high respondent burden and are rarely tested in real-world clinical settings for wide-scale application to learn about patients' experiences. Thus, computer adaptive testing, which may tailor PRO items to individual patient needs, may be considered to reduce patient burden [40, 41]. Two papers [6, 37] discussed the issue of patient burden and both postulated minimisation of patient, clinician, and health care provider burden by limiting frequency and complexity of data collection to a necessary minimum.

Stakeholder collaboration

Collaboration between relevant stakeholders was often mentioned as a key component for the successful use of PROs for RWE generation. According to Calvert et al. [6] international collaboration "…across multiple stakeholders including patients, caregivers, clinicians, regulators, ethicists, industry, payers and policy makers" is needed to establish a standardised approach to PRO assessment for RWE research. This multi-stakeholder collaboration is vital when collecting PRO data for multiple purposes to ensure that the data generated will meet their needs in the future.

Education and training

The importance of educating HCPs, patients, researchers, and other stakeholders on the potential benefits of PROs for RWE generation were mentioned by three publications [34, 35, 38]. Training focused on motivation maintenance and study procedures should be offered to HCPs involved [38]. Kyte et al. [35] recommended that efforts should be made to provide guidance to health care providers and patients on the interpretation and utilisation of benchmarks based on PROs captured in real world setting. Hanson et al. [34] created a searchable outcome measures library (including PRO measures) to educate other researchers interested in designing pragmatic trials in dementia.

PRO implementation process

Five publications [6, 35, 36, 38, 39] gave recommendations specific to the process of PRO implementation. Akiyama et al. [38] described the PRO inclusion process to collect data for post-marketing surveillance. They created a map that covers four stages: internal discussion, design and preparation, implementation, dissemination.

Calvert et al. [6] emphasised that special attention should be given to the resources needed to successfully implement PROs. Additional staff might be required to assist some of the patients with data collection. It is of paramount importance to secure up-front funding to cover costs associated with additional staff time needed, license fees for PRO measures, PRO training, data collection and devices costs. Kyte et al. [35] postulated that a shift to a "bottom-up" clinic-based PRO data collection approach that could be used for multiple purposes may be beneficial for patients and cost containment. Wider utilisation of data collected including post-marketing surveillance was postulated.

The implications of PRO data collection in real-world studies to address the legal requirement for obtaining Clinical Trial Authorisation and being compliant with the EU Clinical Trials Directive were mentioned by The Association of the British Pharmaceutical Industry (ABPI) guidance [39]. When PROs that are not in routine use are to be utilised to obtain data in RWE studies, legislation applicable to interventional clinical trials might need to be followed as PRO data collection can be seen as intervention administrated on the top of the regular care provision. Additionally, Banerjee et al. [36] advocated acceptance of non-medically confirmed adverse events reported by patients to account for more patient-centric approach in post-registration safety surveillance.

Data collection and management

Authors of all seven publications [6, 34–39] made recommendations for data collection and management. The following issues for RWE generation were specifically addressed: frequency of data collection, integration with other databases, data audit, data ownership, electronic data capture and impact of disease progression on data collection.

Frequency of data collection As pointed out by Calvert et al. [6] frequency of data collection depends on stakeholder needs and the study population which should be considered early in study designing process. Additionally, patients with high symptom burden may require more frequent monitoring [6]. Two publications [6, 37] pointed out that the frequency of measurement is influenced by the schedule of patients' visits and poses a challenge for data interpretation. Thus, appropriate methods of PRO measurement which facilitate data interpretation might be needed. Additionally, PRO data capture between scheduled visits could be considered. Calvert et al. [6] advocated the use of alert systems for PRO data collected

between the visits, which would inform HCPs about issues requiring immediate attention. Additionally, reminders sent from electronic data capture systems may facilitate data collection and increase patient retention [38, 42].

Integration with other databases Secondary data collection by integration of data capture with other databases, like electronic health records or registries, was suggested by two papers [6, 34]. Hanson et al. [34] pointed out that EHR systems might be used to facilitate PRO data collection if they had the capability to do so.

Data audit The need for ongoing data quality audit was postulated by Calvert et al. [6]. Moreover, Rylands et al. [37] noted that potentially the amount of missing data, will be influenced by whether PRO data are routinely collected in clinical practice. Moreover, decisions about RWE study design (prospective or retrospective design) may be influenced by whether PROs are routinely collected or not.

Data ownership Issues related to data ownership, storage and access were mentioned by four publications [6, 35, 36, 39]. It should be clearly stated who owns the rights to any data or potential intellectual property generated within the real-world study. Moreover, periods of data retention, entities responsible for their storage and applicable conditions need to be determined *a priori*. Patients should be informed about the way their data will be used and they need to consent to that.

Electronic data capture Five publications [6, 34–36, 38] provided recommendations specific to electronic data capture. All of them advocated the utilisation of electronic capture where appropriate. Akiyama et al. [38] maintained that electronic data collection is suitable for elderly patients and should be used wherever possible, as it streamlines data collection and improves quality of data collected. Electronic data capture can be conducted using the following devices: smartphone or website applications, automated interactive voice response telephone and wearable devices [34]. PRO-enabled website-based platforms were pointed as a preferable data source for collecting information from patients about treatments' safety due to the higher quality of data captured [36]. However, the target population's level of IT literacy should be considered when deciding on the mode of questionnaire administration as this can have serious implications for the representativeness of collected data [6]. Remote delivery of electronic PROs may lead to inequitable access if a substantial proportion of the target population have limited or no access to the internet. These issues could potentially decrease the value of PRO data collected as part of the RWE generation for regulatory purposes and may not be representative. Patients should be provided alternative modes of data collection (e.g., paper questionnaires, automated telephone services).

Impact of disease progression on data collection Three publications [34, 37, 38] commented on changing patient health status over time, and its impact on data collection activities. Hanson et al. [34] highlighted that people living with dementia early in the disease trajectory can self-report. Nevertheless, once the disease progresses there may be a need for transition to proxy reporting, yet no best practices exist for interpretation of data reported by proxy. Similar concerns in the context of elderly patients were expressed by Akiyama et al. [38] Rylands et al. [37] acknowledged that patients' ability to self-report need to be assessed early at the stage of study design.

Data analysis and presentation of results

Four publications [6, 35, 36, 39] provided guidance about results presentation and interpretation. Calvert et al. [6] and Kyte al. [35] provided general recommendations, claiming that data should be analysed and reported appropriately, according to the study objectives and the measure recommendations, following a methodologically robust process. Potential sources of bias and confounding need to be investigated and researchers could offer guidance on how to interpret and utilise findings. Guidance by ABPI [39] stressed how important it is to use sound methods for data generation, cleaning and analysis. Banerjee et al. [36] proposed suitable statistical methods for the analysis of datasets containing information about adverse events, such as appropriate descriptive statistics, methods to address disproportionality of results and multivariate analysis.

Discussion

This review provides the first summary of available guidance for the use of PROs in RWE generation to support regulation, reimbursement, and health policy. Available guidance is fragmented, and it is evident that a better understanding of how to optimally collect and utilise PROs for RWE generation is needed. The main themes generated from the analysis of the included publications addressed issues relating to PRO data collection, analysis, and stakeholder collaboration.

It was recommended that steps should be taken to minimise the burden of PRO data collection on HCPs and patients, [6, 37] reduce data collection errors, allow automatic score calculations, improve data security, and speed up data collection process through the electronic data capture. These would enhance the quality of PROs obtained as part of RWD [23].

Statistical methods for the analysis of collected PRO data were also recommended [36]. Nevertheless, recommendations related to data analysis strategies to manage bias and confounding were not identified as part of this review. The need to develop such guidance seems evident. While existing PRO datasets collected in a real-world setting can be used to inform regulatory or reimbursement processes, a tailored approach to PRO data analysis is key to eliminating biases and confounding. Data captured in the real-world setting might require some additional statistical manipulation to account for inequitable access to PROs (e.g. due to low IT literacy among some groups of patients).

Our review highlighted the need for stakeholders' engagement for successful PRO implementation. To improve efficiency of data collection activities for RWE, collaboration between different stakeholders need to be developed. Each stakeholder might have different expectations from the data collected as they can be used for various purposes. Thus, involvement of various stakeholders early at the stage of research planning is vital. To fully harness the potential benefits of collecting PRO data as part of real-world studies, it was recommended that various issues around stakeholder involvement, instrument selection and implementation need to be resolved [6, 34–38].

The potential benefits of collecting PROs may be maximised by using the data for multiple purposes including trials, routine care, audits, benchmarking and RWE generation [43]. For instance, in routine clinical practice, changes in an individual patient's health status as indicated by their PRO data could facilitate the tailoring of their clinical management, which may, in turn, improve treatment outcomes. The utilisation of PRO alerts informing clinicians about changes in patients' health status may lead to improvement in patient care by providing the opportunity for timely interventions (e.g. earlier clinic appointments or immediate hospitalisation) [43]. The same data can be aggregated for patients within healthcare systems to provide RWE of the safety and tolerability of health interventions. The use of PROs for multiple purposes would require agreement on the measures to be used to meet both regulatory and clinical needs. Feasibility of using the same PRO measures for multiple purposes could be explored further in the future research but it seems to be possible when focusing on aspects such as proximal symptoms and treatment tolerability.

The collection of PRO data in RWE research can bring numerous benefits by providing evidence of long-term safety, tolerability, and effectiveness from the patient perspective. The usefulness of longer-term additional data collection for the purpose of pharmaceutical licensing was previously described in article series by London School of Economics, which considered the use of RWE in Europe [44]. Additionally, the value of data reported directly by patients was evidenced by a comparison of chemotherapy-related adverse events reported by patients and clinicians, where patients tended to self-report more frequent and higher levels of symptoms than clinicians [45].

Although every effort was made to find potentially relevant publications (forwards/backwards citation searches, hand reference list searches, grey literature searches, and website searches were conducted) there is a possibility that some relevant publications were not identified due to poor indexing of the databases and websites searched. A limitation of this work was the dearth of guidance for the use of PROs in RWE to support regulation, reimbursement, and health policy. Even when recommendations were made, in some instances there were limited details on the rationale behind them.

The development of further guidance specific to PROs in RWE generation to support regulation, reimbursement and health policy will be an important next step. In doing so, it is of crucial importance to learn more about the various stakeholders' needs and the current use of PROs in RWE generation to inform the guideline development. Patients, HCPs, regulators, payers, health care providers and industry will bring important perspectives about the specific needs of all those groups. The ISPOR Special Interest Group for Clinical Outcome Assessment is currently working on the standardisation of outcomes for real-world studies. Nevertheless, further research is needed to better inform the development of methodological recommendations for PRO-specific data generation as part of RWE for regulatory, reimbursement, and health policy.

Conclusion

PROs may provide a valuable source of information in RWE generation from the patient perspective. Whilst valuable insights can be gained from guidance for use of PROs in clinical care, there is a lack of international guidance specific to RWE generation in the context of use for regulatory decision-making, reimbursement, and health policy. Clear and appropriate guidance, developed based on evidence, is required to maximise the potential benefits of implementing PROs for RWE generation. Unique aspects between PRO guidance for clinical care and other purposes should be differentiated. This review summarises some recommendations to optimise the use of PROs for RWE generation and highlights the need for further PRO-specific international guidelines to facilitate RWE generation for regulatory, reimbursement, and health policy. The needs of various stakeholder groups

(including patients, health care professionals, regulators, payers, and industry) should be considered when developing future guidelines.

Abbreviations

ABPI: Association of the British Pharmaceutical Industry; AHRQ: Agency for Healthcare Research and Quality; CADTH: Canadian Agency for Drugs & Technologies in Health; EMA: European Medicines Agency; EMBASE: Excerpta Medica Database; FDA: U.S. Food and Drug Administration; HAS: Haute Autorité de Santé; HCP: Health care professionals; HTA: Health technology assessment; ISOP: International Society of Pharmacovigilance; ISOQOL: International Society for Quality of Life Research; ISPOR: Society for Health Economics and Outcomes Research; MEDLINE: Medical Literature Analysis and Retrieval System Online; MHRA: Medicines & Healthcare Products Regulatory Agency; NICE: National Institute for Health and Care Excellence; PCORI: Patient-Centered Outcomes Research Institute; PREMs: Patient-reported experience measures; PRISMA: Preferred Reporting items for systematic reviews and meta-analyses; PROs: Patient-reported outcomes; PROSPERO: International prospective register of systematic reviews; RCT: Randomised control trial; RWE: Real-world evidence; SISAQoL: Standards in Analysing Patient-Reported Outcomes and Quality of Life Endpoints.

Supplementary Information

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Additional file 1: PRISMA 2020 checklist

Additional file 2: Search strategy

Additional file 3: Data extraction

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Author contributions

Conceptualization: MC, OLA, TK, KM. Data Curation: KM, BT. Formal Analysis: KM, BT. Funding Acquisition: MC, OLA, TK. Investigation: KM, BT. Methodology: KM, MC, OLA, TK. Supervision: MC, OLA, TK. Validation: KM, BT. Visualization: KM. Writing–Original Draft Preparation: KM. Writing–Review & Editing: MC, OLA, TK, BT, PC. All authors read and approved the final manuscript.

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Availability of data and materials

All data generated during this study are included in this published article and its supplementary information files. The record of inclusion/exclusion choices is available upon request.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

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Author details

[1]Centre for Patient Reported Outcome Research, Institute of Applied Health Research, University of Birmingham, Birmingham, UK. [2]Birmingham Health Partners Centre for Regulatory Science and Innovation, University of Birmingham, Birmingham, UK. [3]National Institute for Health Research (NIHR) Birmingham Biomedical Research Centre, University of Birmingham, Birmingham, UK. [4]NIHR Surgical Reconstruction and Microbiology Research Centre, University of Birmingham, Birmingham, UK. [5]NIHR Applied Research Collaborative West Midlands, University of Birmingham, Birmingham, UK. [6]GlaxoSmithKline (GSK), Patient Centered Outcome, Value Evidence and Outcomes, Brentford, UK.

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Publisher's Note

Chapter 4: Implementation of patient reported outcome measures in real world evidence studies: Analysis of ClinicalTrials.gov records (1999-2021)

4.1 Introduction

This chapter addresses thesis objective 2: to characterise the current use of PROs in RW studies. Phase IV clinical trials published in the ClinicalTrials.gov database were analysed as they constitute the majority of the RW studies. This study found patterns in the current and past use of PROs in RW studies, PRO utilisation across various clinical areas and use of particular PROMs. Updates to this analysis will allow the monitoring of future trends in the field. The study was published in the Contemporary Clinical Trials (13 August 2022) and is presented below in the journal format.

Appendices 4.1-4.7 contain the following article's supplementary materials:

- Removed search terms (Appendix 1)
- PROMs search term list (Appendix 2)
- Composite measure search term list (Appendix 3)
- Use of PROMs and composite measures in phase IV trials' outcomes (Appendix 4)
- Use of PROMs and composite measures in phase IV trials over time (Appendix 5)
- The 30 most frequently used composite measures (Appendix 6)
- Overview of PROMs mentioned in the manuscript (Appendix 7)

The work has been further disseminated as outlined in Table 4.1.

Table 4.1. Dissemination of publication 2.

Nr	Year	Conference/Publication	Type of communication
1	2022	ISOQOL 29th Annual Conference (Prague)[1]	Poster presentation
2	2023	7th UK Patient Reported Outcome Measures (PROMs) Research Conference (Sheffield)[2]	Poster presentation
3	2023	ISOQOL 30th Annual Conference: Industry SIG symposium (Calgary)[3]	Oral presentation

4.2 References

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2. University of Sheffield. *7th UK Patient Reported Outcome Measures (PROMs) Research Conference: 'PROMs Across the Lifespan'*. 2023; Available from: https://www.sheffield.ac.uk/scharr/7th-uk-patient-reported-outcome-measures-proms-research-conference-proms-across-lifespan.
3. *30th Annual Conference of the International Society for Quality of Life Research.* Quality of Life Research, 2023. **32**(2): p. 23-220.

4.3 Publication 2

Konrad Maruszczyk, Olalekan Lee Aiyegbusi, Victor Roth Cardoso, Georgios V. Gkoutos, Luke T. Slater, Philip Colis, Thomas Keeley, Melanie J. Calvert. Implementation of patient-reported outcome measures in real-world evidence studies: Analysis of ClinicalTrials.gov records (1999–2021). Contemporary Clinical Trials, 2022. 120: p. 106882. https://doi.org/10.1016/j.cct.2022.106882

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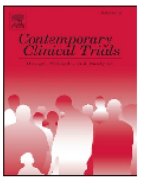

Implementation of patient-reported outcome measures in real-world evidence studies: Analysis of ClinicalTrials.gov records (1999–2021)

Konrad Maruszczyk [a,b], Olalekan Lee Aiyegbusi [a,b,c,d,e,*], Victor Roth Cardoso [f], Georgios V. Gkoutos [f], Luke T. Slater [f], Philip Collis [a,e,g], Thomas Keeley [a,h], Melanie J. Calvert [a,b,c,d,e]

[a] Centre for Patient Reported Outcome Research, Institute of Applied Health Research, University of Birmingham, Birmingham, UK
[b] Birmingham Health Partners Centre for Regulatory Science and Innovation, University of Birmingham, Birmingham, UK
[c] National Institute for Health and Care Research (NIHR) Birmingham Biomedical Research Centre, University of Birmingham, Birmingham, UK
[d] NIHR Surgical Reconstruction and Microbiology Research Centre, University of Birmingham, Birmingham, UK
[e] NIHR Applied Research Collaboration (ARC) West Midlands, University of Birmingham, Birmingham, UK
[f] Institute of Cancer and Genomic Sciences, University of Birmingham, Birmingham, UK
[g] Patient partner, UK
[h] GlaxoSmithKline (GSK), Patient Centered Outcome, Value Evidence and Outcomes, Brentford, UK

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ABSTRACT

Background: Real-world evidence (RWE) plays an increasingly important role within global regulatory and reimbursement processes. RWE generation can be enhanced by collecting and using patient-reported outcomes (PROs), which can provide valuable information on the effectiveness, safety, and tolerability of health interventions from the patient perspective. This analysis aims to examine and summarise the utilisation of patient-reported outcomes measures (PROMs) in real-world studies.

Methods: Descriptions of phase IV trials were downloaded on July 22, 2021 from the Clinicaltrials.gov database since its inception. An automated algorithm was built to detect trials utilising PROMs and composite measures including patient-reported components. Search terms were developed based on the PROQOLID database.

Results: Of 27,976 phase IV clinical trials posted on Clinicaltrials.gov between 1999 and July 2021, 21% and 4% used PROMs and composite measures, respectively. Recent years demonstrated a steady increase in the utilisation of PROMs in phase IV trials.

Conclusions: The use of PROMs in phase IV trials seems to be lower than its use in earlier phases of clinical research. Increased uptake of PROMs in RWE studies can be facilitated in a number of ways including the development of standards for their collection, analysis and use.

1. Introduction

Real-world evidence (RWE) is increasingly used to support regulatory and reimbursement decision-making processes globally [1,2]. The U.S. Food and Drug Administration (FDA) published a framework for Real-World Evidence [3], which was recently supplemented by four real-world data (RWD) draft guidelines on data sources, data standards, and regulatory considerations [4–7]. In the UK, the Medicines & Healthcare products Regulatory Agency (MHRA) recently issued two guideline documents focusing on the utilisation of RWD to support regulatory decisions [8,9]. Moreover, the National Institute for Health and Care Excellence draft real-world evidence framework is currently available for public consultation [10]. The European Medicines Agency (EMA) currently uses RWE for safety monitoring and recently announced that the use of RWE will be established across its spectrum of regulatory use cases by 2025 [11].

Contrary to the highly controlled environment of phase III

Abbreviations: COA, clinical outcome assessments; EMA, The European Medicines Agency; ePRO, electronic patient-reported outcome; FDA, U.S. Food and Drug Administration; MHRA, The Medicines & Healthcare products Regulatory Agency; PRO, patient-reported outcome; PROM, patient-reported outcome measure; PROQOLID, Patient-Reported Outcome and Quality of Life Instruments Database; RWD, real-world data; RWE, real-world evidence; XML, Extensible Markup Language.

* Corresponding author at: Murray Learning Centre, Edgbaston, Birmingham B15 2TT, UK.
E-mail address: o.l.aiyegbusi@bham.ac.uk (O.L. Aiyegbusi).

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Box 1
Lay summary.

One way to assess the impact of medical treatments is to assess the impact they have on patient symptoms and quality of life. Patient symptom and quality of life data are increasingly collected in clinical trials to assess whether treatments are safe and work. Once treatments have received regulatory approval for use it is important to assess longer term patient outcomes. This could include real-world impact on symptoms and quality of life.

Using data from an international registry this research paper investigates the evidence of the use of patient-reported outcomes, such as symptom and quality of life data, to provide real-world evidence of the safety and effectiveness of therapies. The research shows an increase in use over time from 1999 to 2021. However, the research shows that collection of data in this setting is still quite low, suggesting the need to further develop the methods of data collection.

registration trials (i.e. to establish an acceptable benefit/safety profile in order to seek regulatory approval for a precisely defined indication), which are usually characterised by close patient monitoring and artificially high patient compliance, RWE studies are characterised by less constrained inclusion criteria and usually, involve a greater number of diverse participants [12]. By evaluating health interventions among diverse, large, and heterogeneous patient populations, RWE studies provide a better understanding of their real-world effectiveness, safety, and tolerability. RWE can therefore inform regulatory decisions, reimbursement, and health policy-making purposes. RWE can be generated through various study designs by analysing real-world data (RWD). Both prospective and retrospective data collection can be utilised to inform RWE generation. The most common sources of RWD are electronic health records, claims databases, registries, and patient-generated data [13].

Patient-reported outcomes (PROs) are reports of health status or quality of life directly provided by patients, without interpretation by a clinician or anyone else [14]. Therefore, PROs provide a unique and valuable source of information and are usually assessed using patient-reported outcome measures (PROMs) – validated measurement tools mainly in a form of questionnaires. Moreover, composite measures are used, incorporating multiple clinical outcome assessments (COAs), including patient-reported ones. PROMs and composite measures are routinely captured within RCTs, primarily to inform regulatory and reimbursement processes [15]. Recently, global regulators, payers, and policymakers have increasingly recognised that PROs can provide valuable information on the effectiveness, safety, and tolerability of drugs from the patient perspective [15–18]. The Framework for FDA's Real-World Evidence Program [3] highlights the use of PROs in RWE generation by acknowledging that PROs provide unique and valuable information which may complement the evidence obtained using traditional clinician-focused parameters [3]. This increased interest in collecting PROs to enrich RWD can be seen as part of a commitment to strengthen patient-centricity in drug development processes.

Recent developments in health informatics infrastructure allow for the use of electronic PROs (ePROs). PROs are being collected in routine care to facilitate individual-level treatment decisions and to support disease progression monitoring. Despite this, PRO data collection in real-world settings remains limited. It seems that broader adoption of PROs for RWE generation could be facilitated by setting up standards for data collection, analysis, and use. In a commentary article, Calvert and colleagues [15] pointed out several priorities. Addressing them would make it possible to fully benefit from the use of PROs in RWE generation. They also called for efforts to advance the understanding of successful PRO implementation in RWE studies. The lack of international guidelines to facilitate the use of PROs in RWE studies was highlighted by a recent systematic review [19].

To inform the development of best practice guidance for PRO data utilisation in RWE generation, it is crucial to understand better how PROMs are currently being used and how this has evolved over time. One possible approach to determine PROMs utilisation is to scrutinise trial registers available in the public domain. Most of the journals require authors to register their studies in publicly available databases prior to the publication of study results. Clinicltrials.gov is a commonly used database for the registration of trials. This database was previously used to assess PROMs utilisation at two time periods: 2004–2007 and 2007–2013 by Scoggins and Patrick [20], and Vodicka et al. [21], respectively. Both studies investigated the use of PROMs in all registered clinical trials, but the latter one focused on utilisation of PROMs in oncological trials. Both forementioned studies are now outdated, and they did not explicitly focus on RWE studies. Thus, there is a need to conduct an up-to-date analysis of Clinicaltrials.gov records, focusing on RWE studies. This will provide an understanding of the current picture of PROMs' use and support future endeavours to facilitate the broader implementation of PROMs in RWE generation.

The research objectives were: (1) quantify the usage of PROMs and composite measures in RWE studies (phase IV trials), (2) describe their utilisation patterns over time and (3) investigate the use of PROMs and composite measures across different disease areas in phase IV trials. An automated searching algorithm was used to identify phase IV studies registered in ClinicalTrial.gov, which report PROMs and composite measures.

2. Materials and methods

The methodology adopted by this study built on the previous analyses of the Clinicaltrials.gov database by Vodicka et al. [21]. Nevertheless, the searching algorithm was developed de novo. The search term list was constructed based on the PROQOLID (Patient-Reported Outcome and Quality of Life Instruments Database), including PROMs and composite measures, including a patient-reported component.

2.1. *Clinicaltrials.gov database*

The Clinicaltrials.gov database holds information provided by researchers about the studies they plan to conduct. High-level trial characteristics, along with details about outcomes assessed within the studies, are stored on the database. Clinicaltrials.gov website allows users to download a complete record of all trials registered on the database. Records are made available in the form of the Extensible Markup Language (XML) files. On July 22, 2021 Clinicaltrials.gov database snapshot, since its inception, was downloaded. The scope of this paper is solely on RWE studies. The database allows filtering records by stage of a clinical trial, based on definitions developed by the FDA. Our search was restricted to phase IV studies only. This filter was deemed the most appropriate to use, although RWE can be generated by multiple study designs and might be considered as a broader term than "phase IV clinical trials". As a result, records of 27,976 trials were made available for further analysis. Studies included in the analysis reported 159,386 outcomes, as a single study can assess multiple outcomes. The following outcome types are differentiated in the Clinicaltrial.gov database: "primary", "secondary", and "other". Apart from trial

outcomes, high-level trial characteristics were also extracted, including trial ID, first posted date, condition, intervention type, lead sponsor, and country information.

2.2. Search terms lists

The PROQOLID database, part of the ePROVIDE platform, that gathers information about COAs available for use in medical research [22], was used to create the list of search terms. PROQOLID database since its inception in 2002 gathered information about more than five thousand COAs. It was created to facilitate the search, evaluation and selection of appropriate COAs. PROQOLID is the most comprehensive database of PROMs and composite measures and also holds their descriptive information.

Filters embedded in the PROQOLID database allow searching for specific types of outcomes. The database distinguishes the following types of COAs: patient-reported, clinician-reported, observer-reported and performance outcome assessments. Additionally, a composite measure category is available, containing instruments that fall under more than one of the above categories. For this study, two separate search terms lists were created. The first one was constructed using the "PRO" filter, while the second used the "Composite measure" filter to identify measures with patient-reported component.

On July 19, 2021 search term lists were manually copied from the PROQOLID website resulting in 2806 PROMs and 182 composite measure records. For each instrument, the full and abbreviated names were captured as they appeared in the PROQOLID database. To ensure that all relevant trials were identified, even when ClinicalTrials.gov record does not mention exact PROM's name in the outcome description or mentioned name differs from the one in the search term list, the following phrases were added to the PROM search term list: "Quality of life" and "eq5d". Moreover, some abbreviated names of instruments were manually removed from the lists while retaining the full instrument names to increase the searching algorithm specificity. The terms that most frequently resulted in false-positive instrument identification were removed – 33 terms from the PRO list and three from the composite measure list. A list of removed terms is available in the Appendix 1. Complete lists of PROMs and Composite measures search terms are available in Appendixs 2 and 3, respectively.

2.3. Trial characteristics grouping

Conditions investigated in trials are reported as free-text information on ClinicalTrials.gov. Additionally, a list of all conditions grouped into 23 categories is available on the ClinicalTrials.gov website [23]. For this analysis, we adopted the ClinicalTrials.gov disease area grouping. A newly created category "Multimorbidity" was assigned to trials investigating conditions included in more than one group.

Similarly, ClinicalTrials.gov grouping was utilised for intervention type, lead sponsor and region. For intervention type and lead sponsor, additional categories – "Multiple interventions/sponsors" – were created in case more than one intervention/sponsor type was reported for the study. Indexing on ClinicalTrials.gov was not complete; in such instances when a missing value for a trial characteristic was present or the algorithm developed to assign groups to free-text fields was unable to do so based on the information provided on the ClinicalTrials.gov website, "N/A" value was assigned for that variable.

2.4. Searching algorithm development and validation

A computer algorithm was developed de novo to search the ClinicalTrials.gov database snapshot against the full and abbreviated names of instruments stored in search terms lists from PROQOLID. Data compilation and processing were done in Python version 3.8.8 using exact matching. Although alternative approaches were tested including: fuzzy string matching algorithm [24] (matches the sentences using Levenshtein Distance [25]), word ratio (calculates ratio of words that are similar between the compared terms), word2vec [26] (counts words for each term into a vector), and TF-IDF [27] (counts words for each term into a vector but the most important words weight more). Each outcome and its description reported in the ClinicalTrials.gov were matched against up to five terms from search term lists (to capture multiple instruments reported within a single trial outcome).

The Python algorithm was iteratively revised to increase its accuracy by altering algorithm settings. Those settings pertained various approaches to text transformation, length of compared text strings and inclusion of outcome description in searching. For the final analysis, the searching algorithm ignored capitalisation, removed any punctuation, and added spaces before and after searched terms to avoid finding phrases of interest within some other words (e.g. "SOC", which often was identified within the word "social").

Table 1
Search algorithm validation parameters.

	PROMs (%)	Composite measures (%)
Sensitivity	88.3	83.3
Specificity	98.6	98.8
Accuracy	97.6	98.6
PPV	86.5	45.5
NPV	98.8	99.8

PPV, positive predictive value; NPV, negative predictive value.

3. Results

Records of 27,976 phase IV trials were downloaded for analysis. The trials assessed 159,386 outcomes, of which 43,150 were primary and 109,410 secondary outcomes. The remaining 6826 were classified as other outcomes.

The performance of the searching algorithm was evaluated by manual cross-checking by one researcher (KM). A sample of trial records (108 most recently published and 31 oldest records) was screened for the existence of outcomes utilising PROMs or composite measures present in search terms lists. KM evaluated 1003 (0.6%) outcomes from 139 (0.5%) trials. Outcomes flagged by the algorithm as containing at least one instrument of interest were compared to the manual screening conducted by the researcher. The sensitivity and specificity of searching algorithm were calculated. For the PROMs search, sensitivity was 88.3% and specificity 98.6%. Sensitivity and specificity yielded 83.3% and 98.8% respectively for composite measure search (Table 1). Accuracy of the algorithm for both outcome types was higher than the one obtained by Vodicka et al. [21] and was deemed satisfactory. Outcomes incorrectly identified as PROMs or composite measures (false positives) were mainly picked up in two ways: 1) the outcome name or description included on ClinicalTrials.gov matched a term from the PROQOLID list, but in fact did not refer to that measure or instrument listed in PROQOLID. Instead, this referred to a measure with the same name (e.g. National Comorbidity Survey and Nerve Conduction Studies are both written as NCS in the abbreviated form); 2) an outcome reported on clinicaltrials.gov matched a term in PROQOLID, but additional information provided in the ClinicalTrials.gov record indicated that this had been completed by a proxy (parent or teacher of a child). In turn, PROMs or composite measures that algorithm failed to identify (false negatives) were mostly caused by differences in how instrument full name was written and lack of abbreviated name in outcome description.

Out of 159,386 outcomes analysed, 8% assessed at least one PROM. Slightly more than 1% of outcomes were composite measures, including patient-reported component. PROMs were mostly investigated as secondary outcomes, and almost 9% of secondary outcomes utilised PROMs. Counts of trials outcomes utilising PROMs and composite measures are available in Appendix 4.

Out of 27,976 phase IV trials analysed, almost 21% collected at least

Table 2
Use of PROs and composite measures in phase IV trials.

	Number of trials reporting instrument (%)		Number of trials
	PROMs	Composite measures	
Trials reporting at least one instrument	5812 (20.77)	1105 (3.95)	27,976
Trials reporting at least one instrument as primary outcome	1906 (6.81)	436 (1.56)	27,969*
Trials reporting at least one instrument as secondary outcome	4561 (19.94)	797 (3.48)	22,870#
Intervention			
Behavioral	61 (27.6)	8 (3.62)	221
Biological	117 (11.54)	35 (3.45)	1014
Combination Product	14 (22.95)	3 (4.92)	61
Device	355 (22.54)	37 (2.35)	1575
Diagnostic Test	5 (19.23)	0 (0)	26
Dietary Supplement	63 (18.1)	9 (2.59)	348
Drug	3885 (20)	789 (4.06)	19,427
Genetic	3 (33.33)	1 (11.11)	9
Multiple interventions	942 (26.54)	181 (5.1)	3549
Other	152 (22.96)	19 (2.87)	662
Procedure	196 (19.72)	20 (2.01)	994
Radiation	3 (12.5)	0 (0)	24
N/A	16 (24.24)	3 (4.55)	66
Lead sponsor type			
Clinical Research Network	26 (18.98)	6 (4.38)	137
Government, excluding U.S. Federal	125 (15.66)	24 (3.01)	798
Industry	1650 (26.46)	292 (4.68)	6235
National Institute of Health	17 (16.67)	7 (6.86)	102
U.S. Federal Agency, excluding NIH	55 (21.74)	12 (4.74)	253
University/Organization	3503 (18.94)	673 (3.64)	18,497
N/A	436 (22.31)	91 (4.66)	1954
Region			
Africa	67 (7)	8 (0.84)	957
Central America	2 (9.52)	2 (9.52)	21
East Asia	688 (17.11)	159 (3.96)	4020
Europe	1544 (22.36)	287 (4.16)	6906
Middle East	104 (10.77)	22 (2.28)	966
Multiple regions	408 (32.61)	104 (8.31)	1251
North America	2137 (23.19)	380 (4.12)	9214
North Asia	42 (25.45)	7 (4.24)	165
Pacifica	56 (25.93)	9 (4.17)	216
South America	153 (19.01)	21 (2.61)	805
South Asia	63 (14.96)	13 (3.09)	421
Southeast Asia	98 (19.56)	8 (1.6)	501
N/A	450 (17.77)	8 (3.36)	2533
Disease group			
Behaviors and Mental Disorders	597 (43.8)	123 (9.02)	1363
Blood and Lymph Conditions	63 (22.26)	1 (0.35)	283
Digestive System Diseases	162 (15.07)	52 (4.84)	1075
Diseases and Abnormalities at or Before Birth	55 (23.11)	40 (16.81)	238
Ear, Nose, and Throat Diseases	62 (36.26)	6 (3.51)	171
Eye Diseases	80 (13.18)	1 (0.16)	607
Gland and Hormone Related Diseases	138 (14.84)	3 (0.32)	930
Heart and Blood Diseases	323 (14.76)	75 (3.43)	2189
Immune System Diseases	313 (32.95)	181 (19.05)	950
Infections	80 (8.94)	16 (1.79)	895
Mouth and Tooth Diseases	28 (14.74)	2 (1.05)	190
Multimorbidity	337 (23.42)	46 (3.2)	1439
Musculoskeletal Diseases	268 (45.58)	36 (6.12)	588
Neoplasms	41 (22.78)	1 (0.56)	180
Nervous System Diseases	126 (36.21)	35 (10.06)	348
Nutritional and Metabolic Diseases	53 (10.1)	5 (0.95)	525
Respiratory Tract (Lung and Bronchial) Diseases	117 (37.26)	13 (4.14)	314
Skin and Connective Tissue Diseases	69 (24.56)	4 (1.42)	281
Substance Related Disorders	2 (15.38)	0 (0)	13
Symptoms and General Pathology	357 (19.91)	24 (1.34)	1793
Urinary Tract, Sexual Organs, and Pregnancy Conditions	45 (9.43)	1 (0.21)	477
Wounds and Injuries	21 (21)	3 (3)	100
N/A	2475 (19)	437 (3.35)	13,027

* Represents the total number of trials which assessed primary outcomes. Descriptions of seven trials did not contain information about the primary endpoint. It was most likely caused by data errors in the Clinicaltrials.gov database.

Represents a total number of trials which assessed secondary outcomes.

one PROM. At least one composite measure was assessed by nearly 4% of investigated trials (Table 2). Both PROMs and composite measures tended to be assessed as secondary outcomes. The utilisation of PROMs among phase IV trials did not vary greatly between different types of interventions being assessed. The greatest variation was observed in trials investigating biological, genetic and radiation intervention types, but this might be due to a relatively small number of trials grouped in these categories. Trials focusing on biological and radiological interventions assessed PROMs significantly less frequently than on average. On the other hand, PROMs were often collected to investigate genetic treatments. PROMs were most often collected as part of industry-sponsored phase IV trials when compared with other types of lead sponsors. The lowest penetration of PROMs in the phase IV trials was observed in Africa, Central America, and the Middle East.

Despite a substantial quantity of missing data that prevented the identification of disease categories for almost half of the trials included in the analysis, some areas of the most extensive use of PROMs can be described (Table 2). Trials focusing on: Behaviors and Mental Disorders, Ear, Nose, and Throat Diseases, Nervous System Diseases, and

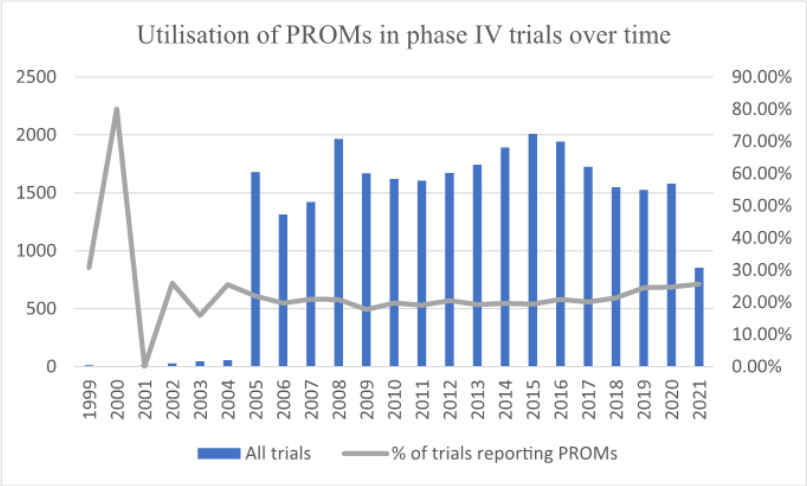

Fig. 1. The utilisation of PROMs in phase IV trials over time.

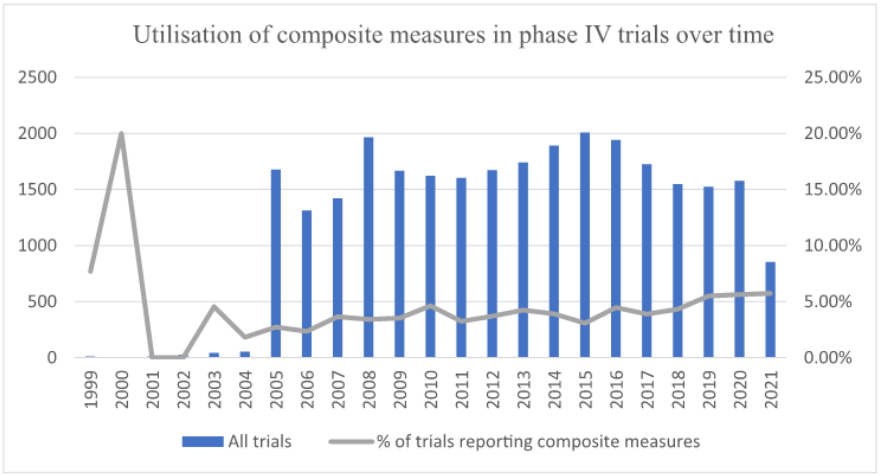

Fig. 2. The utilisation of composite measures in phase IV trials over time.

Respiratory Tract (Lung and Bronchial) Diseases were more likely to collect this type of data. Trials focusing on Infections, Nutritional and Metabolic Diseases, and Urinary Tract, Sexual Organs, and Pregnancy Conditions collected PROMs least often.

A stable level of utilisation for both PROMs and composite measures can be observed since 2005 (Appendix 5). A considerable variation in instruments utilisation was observed before 2005, which might be caused by a low number of trials posted in this period. An increase in PROMs uptake in phase IV trials can be observed since 2019 (*Fig.* 1). Similarly, increase in the utilisation of composite measures was captured since 2019 (Fig. *2*).

Table 3 presents 30 of the most frequently used PROMs. "Quality of life" search term is an umbrella term that picked out PROs that were not specified with exact instrument names but mentioned assessing patients' quality of life. Additionally, trials utilising different types of EQ-5D questionnaires (e.g. EQ-5D-3 L, EQ-5D-5L) were aggregated into a common category. The top five most frequently utilised composite measures included: Pittsburgh Sleep Quality Index, Bleeding Academic Research Consortium Scale, American College of Rheumatology, Diagnostic and Statistical Manual of Mental Disorders, Unified Parkinson's Disease Rating Scale (Appendix 6).

4. Discussion

Of phase IV clinical trials posted on Clinicaltrials.gov between 1999 and July 2021, 21% and 4% used PROMs and composite measures, respectively. Our findings imply a slightly lower utilisation of PROMs than one described by Vodicka et al. [21] (27%). Their analysis covered 2007–2013 and was not restricted only to phase IV studies. These results might suggest lower penetration of PROMs among phase IV studies when compared to earlier phases. The reason for limited widespread of PROMs among phase IV trials is unclear but may be associated with greater difficulties encountered in PRO data collection in a real-world setting and a lack of consensus for optimal data collection and analyses. Collecting PROs is related to additional burden on healthcare professionals, require adjustments to clinical pathways and generate additional costs. Moreover, especially remote utilisation of PROMs is based on patients' compliance and their willingness to provide data which sometimes might be challenging. Mentioned examples offer just a few possible hurdles associated with the use of PROMs in real-world

Table 3
The 30 most frequently used PROMs.

Measure	Number of trials (%)
Quality of Life (umbrella term)	1297 (4.64)
SF-36 Health Survey	507 (1.81)
EQ-5D (sum for different questionnaire versions)	429 (1.53)
Montgomery-Asberg Depression Rating Scale	195 (0.7)
Western Ontario and McMaster Universities Arthritis Index	148 (0.53)
Brief Pain Inventory	138 (0.49)
Health Assessment Questionnaire	127 (0.45)
Hospital Anxiety and Depression Scale	126 (0.45)
SF-12 Health Survey	124 (0.44)
Dermatology Life Quality Index	117 (0.42)
Life Quality Index	103 (0.37)
Epworth Sleepiness Scale	95 (0.34)
Asthma Control Test	95 (0.34)
Pain Catastrophizing Scale	92 (0.33)
International Index of Erectile Function	86 (0.31)
COPD Assessment Test	77 (0.28)
Oswestry Disability Index	74 (0.26)
Balanced Inventory for Spinal disorders	72 (0.26)
International Prostate Symptom Score	71 (0.25)
Quality of Life Scale	64 (0.23)
Ocular Surface Disease Index	63 (0.23)
Severity of Dependence Scale	62 (0.22)
Knee Injury and Osteoarthritis Outcome Score	57 (0.2)
Sheehan Disability Scale	55 (0.2)
Beck Depression Inventory - Second Edition	53 (0.19)
Kansas City Cardiomyopathy Questionnaire	51 (0.18)
Total Symptom Score	51 (0.18)
St George's Respiratory Questionnaire	49 (0.18)
Patient Health Questionnaire	47 (0.17)
Total Nasal Symptom Score	46 (0.16)

settings, which holds back their full implementation. Undoubtedly, more issues need to be resolved, and additional guidance how to tackle these is required. The uptake of PROMs in RWE generation can be stimulated by initiatives aiming to produce guidance on methodologies for data collection, analysis and PRO data use. International agreement upon standards for PROMs' utilisation should facilitate its uptake in RWE generation. The regulators (MHRA, FDA or EMA) or international societies (The International Society for Health Economics and Outcomes Research or International Society for Quality of Life Research) have an essential role in promoting PROs for RWE generation. Guidelines for PRO data collection and utilisation should increase their use in real-world studies.

Our findings depicted a relatively steady uptake of PROMs in phase IV clinical trials from 2005 to 2019. A gradual increase in the utilisation of this type of outcome was observed from 2019. An increase in the utilisation of PROMs over time was also captured by previous studies, which were not restricted to phase IV trials. The earlier analysis of Clinicaltrials.gov records by Scoggins and Patrick [20], which spanned between 2004 and 2007, reported that 14% of trials used at least one PROM. This constitutes a significant increase in PROMs' utilisation since 1997, when Sanders [23] observed that only 4.2% of studies used it. A similar percentage (4.4%) was observed by Naito et al. [23] among Japanese trials between 2000 and 2003.

Several important limitations merit discussion. Although our primary interest is in RWE, we were forced to focus on phase IV trials only in this analysis. Due to the indexing of Clinicaltrials.gov database, the trial phase was applied to filter records. RWE can be generated using different study designs and is undoubtedly a broader term than the phase IV trial. This can be seen as one of the limitations of this study. Nevertheless, in our opinion, the main observations - limited use of PROMs when compared with earlier phases trials - can be extrapolated to the entire body of RWE. Another limitation of this study is the US-focused nature of Clinicaltrials.gov database. Thus, studies conducted in some geographies might be overlooked. Nevertheless, as already presented in Table 2, our approach allowed for international coverage of trials included into analysis. Moreover, missing field completion on the database hampered analysis of some of the trial characteristics of interest. This was particularly visible when summarising conditions targeted by individual studies.

Additionally, the use of a searching algorithm imposed some challenges and although this may not be as accurate as manual records screening, this approach allowed for analysis of the large sample size, which would have been difficult manually. In addition, the algorithm can be easily replicated on other data sets. The method utilised in this study allows for identifying only these measures, which are indexed in PROQOLID. Thus, our results might slightly underestimate the actual uptake of PROMs and composite measures in phase IV trials, mainly when investigators have used non-specific terminology around symptom assessment and measurement scales. Improved labelling of trial outcomes by clear defining the PROMs would facilitate indexing and registration on Clinicaltrials.gov. This would certainly enhance the execution of similar research in the future. Another limitation of this study is associated with the fact that trials' outcomes captured in the Clinicaltrials.gov database might not accurately represent clinical trial protocols. Again, improvements in reporting to the database should allow for more robust conclusions drawn from this type of research in the future.

5. Conclusions

In conclusion, the use of PROMs in phase IV trials seems to be lower than its use in earlier phases of clinical research. Recent years demonstrated a steady increase in the utilisation of PROMs in phase IV trials. A number of initiatives can be developed to improve the incorporation of PROMs in RWE studies including the development of best practices for their use and highlighting needs of regulators and payers.

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CRediT authorship contribution statement

Konrad Maruszczyk: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Visualization, Writing – original draft. **Olalekan Lee Aiyegbusi:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. **Victor Roth Cardoso:** Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Writing – review & editing. **Georgios V. Gkoutos:** Formal analysis, Methodology, Resources, Software, Writing – review & editing. **Luke T. Slater:** Data curation, Formal analysis, Investigation, Methodology, Resources, Software, Writing – review & editing. **Philip Collis:** Methodology, Writing – review & editing. **Thomas Keeley:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing. **Melanie J. Calvert:** Conceptualization, Funding acquisition, Methodology, Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

MC is Director of the Birmingham Health Partners Centre for Regulatory Science and Innovation, Director of the Centre for Patient-Reported Outcomes Research and is a National Institute for Health and Care Research (NIHR) Senior Investigator. She receives funding from the NIHR Birmingham Biomedical Research Centre, the NIHR Surgical Reconstruction and Microbiology Research Centre and NIHR Applied Research Collaboration (ARC) West Midlands at the University

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Other authors declare no competing interests.

The views expressed in this article are those of the authors and not necessarily those of the NIHR, or the Department of Health and Social Care.

Data availability

Data will be made available on request.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.cct.2022.106882.

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Chapter 5: Qualitative Interviews to Identify Considerations for Wider Implementation of Patient Reported Outcomes in RWE Generation

5.1 Introduction

This chapter addresses thesis objectives 2-4 of the thesis: to characterise the current use of PROs in RW studies, to explore in-depth perspectives of international stakeholders about challenges and opportunities for using RW-PROs and to identify strategies enhancing the uptake of PROs in the RWE generation.

It was published in Heliyon (14th September 2023) and is presented below in the journal format.

This study was recognised with **the best poster presentation award at the 7th UK Patient Reported Outcome Measures (PROMs) Research Conference.**

Appendices 5.1-5.3 contain the following article's supplementary materials:

- Patient experts' interview topic guide (Appendix 1)
- Other experts' interview topic guide (Appendix 2)
- Summary of key findings – CFIR domains, belief statements and representative quotes (Appendix 3)

The work has been further disseminated as outlined in Table 5.1.

Table 5.1. Dissemination of publication 3.

Nr	Year	Conference/Publication	Type of communication
1	2022	ISPOR Europe 2022 (Vienna)[1]	Poster presentation
2	2023	ISOQOL 30th Annual Conference: Industry SIG symposium (Calgary)[2]	Oral presentation
3	2023	ISOQOL 30th Annual Conference (Calgary)[2]	Oral presentation
4	2023	The Evidence Base: Peek Behind the Paper[3]	Interview
5	2024	7th UK Patient Reported Outcome Measures (PROMs) Research Conference (Exeter)[4]	Poster presentation

5.2 References

1. Maruszczyk, K., et al., *PCR171 Considerations for Successful Implementation of Patient-Reported Outcomes in Real-World Evidence Generation: Interviews With Patients and Stakeholders.* Value in Health, 2022. **25**(12, Supplement): p. S424.
2. *30th Annual Conference of the International Society for Quality of Life Research.* Quality of Life Research, 2023. **32**(2): p. 23-220.
3. Maruszczyk, K. *Peek Behind the Paper: Considerations for the wider implementation of patient-reported outcomes in real-world evidence generation*. The Evidence Base 2023; Available from: https://www.evidencebaseonline.com/peek-behind-the-paper-considerations-for-the-wider-implementation-of-patient-reported-outcomes-in-real-world-evidence-generation/.
4. University of Exeter. *8th National Patient Reported Outcome Measures (PROMs) Research Conference*. 2024 28/05/2024]; Available from: https://medicine.exeter.ac.uk/events/proms24/.

5.3 Publication 3

Konrad Maruszczyk, Christel McMullan, Olalekan Lee Aiyegbusi, Thomas Keeley, Roger Wilson, Philip Colis, Catherine Bottomley, Melanie J. Calvert. Paving the way for patient centricity in real-world evidence (RWE): Qualitative interviews to identify considerations for wider implementation of patient-reported outcomes in RWE generation. Heliyon, 2023. 9(9): p. e20157. https://doi.org/10.1016/j.heliyon.2023.e20157

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Paving the way for patient centricity in real-world evidence (RWE): Qualitative interviews to identify considerations for wider implementation of patient-reported outcomes in RWE generation

Konrad Maruszczyk [a], Christel McMullan [a,b], Olalekan Lee Aiyegbusi [a,c,*], Thomas Keeley [a,d], Roger Wilson [a,e], Philip Collis [a,e], Catherine Bottomley [f], Melanie J. Calvert [a,g]

[a] *Centre for Patient Reported Outcome Research and Birmingham Health Partners Centre for Regulatory Science and Innovation, University of Birmingham, Birmingham, UK*
[b] *NIHR Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics, University of Birmingham, Birmingham, UK*
[c] *NIHR Applied Research Collaboration (ARC) West Midlands, University of Birmingham, Birmingham, UK*
[d] *GlaxoSmithKline (GSK), Patient Centered Outcomes, Value Evidence and Outcomes, Brentford, UK*
[e] *Patient partner, UK*
[f] *Vitaccess Ltd., Oxford, UK*
[g] *NIHR Birmingham Biomedical Research Centre, University of Birmingham, Birmingham, UK*

A B S T R A C T

Objectives: Real-world evidence (RWE) generation can be enhanced by including patient-reported outcomes (PROs). Methods for collecting and using PRO data in the real-world setting are currently underdeveloped and there is no international guidance specific to its use in this context. This study explored stakeholders' perspectives and needs for using PROs in RWE generation. Barriers, facilitators, and opportunities for wider use of PROs in real-world studies were also investigated.

Methods: Online semi-structured interviews were conducted with international stakeholders: patients, patient advocates, regulators, payers, clinicians, academic researchers, and industry experts. Interviews were recorded, transcribed verbatim and analysed using NVivo 20. Thematic analysis was conducted based on the updated Consolidated Framework for Implementation Research (CFIR).

Results: Twenty-three interviews were conducted. Participants confirmed that the use of PROs in RWE generation is not yet well established. Participants expressed a mixed level of confidence in the value of PROs collected in a real-world setting. Operational challenges associated with collecting routine PRO data to inform care delivery at the individual level (e.g., setting up infrastructure) need to be addressed. Methodological and other challenges (e.g., financing research) associated with collecting prospective *de novo* data in a real-world setting should be considered to facilitate PRO utilisation in real-world studies.

Conclusions: Several opportunities and challenges were identified regarding the broader use of PROs in RWE research. Joint efforts from different stakeholders are needed to maximise PRO implementation, with consideration given to each stakeholders' specific needs (e.g., by developing good practices).

* Corresponding author. Centre for Patient Reported Outcome Research, Institute of Applied Health Research, University of Birmingham, Murray Learning Centre Edgbaston, Birmingham, B15 2TT, UK.
E-mail address: o.l.aiyegbusi@bham.ac.uk (O.L. Aiyegbusi).

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Box 1
Glossary

Clinical outcome assessment (COA) [65] – a clinical evaluation instrument that is used to measure patient outcomes. There are four types of COAs: patient-reported outcomes, clinician-reported outcomes, observer-reported outcomes, and performance-based outcomes assessments.
Managed Access Programme [66] - a time-limited agreement that sets out conditions under which treatment will be reimbursed, including rules for data collection to address the uncertainties related to the effectiveness or cost-effectiveness of a treatment.
Patient-reported outcome (PRO) [21] - Reports of health status directly provided by patients, without interpretation by a clinician or anyone else. One of the types of COA.
Real-world data (RWD) [13] - Data relating to patient health or experience or care delivery collected outside the context of a highly controlled clinical trial. RWD can be routinely collected during the delivery of health or social care or can be collected prospectively to address specific research question(s). It can come from many different sources, including patient health records, administrative records, patient registries, surveys, observational cohort studies and digital health technologies.
Real-world evidence (RWE) [67] - Evidence generated from the analysis of real-world data.

1. Introduction

Real-world evidence (RWE), as defined in Box 1, plays an increasingly prominent role in regulatory decisions, reimbursement and formulation of health policies [1–6]. Analysis of real-world data (RWD) (see Box 1) can provide information about health interventions' long-term tolerability, effectiveness and safety. Different study designs, including both prospective and retrospective data collection, could be used to generate RWE [7]. These studies are characterised by less stringent patient eligibility criteria than those required for registration purposes. Real-world studies allow for the investigation of diverse, large and heterogeneous patient populations. Recently published guidance and frameworks confirmed the growing interest in RWE globally. The US Food and Drug Administration (FDA) issued a framework for RWE [8], recently supplemented with four draft FDA RWE guidelines on data sources, standards, and regulatory considerations [9–12]. In the UK, the National Institute for Health and Care Excellence (NICE) has published a RWE framework [13] and the Medicines & Healthcare products Regulatory Agency (MHRA) has issued two guideline documents focusing on using RWD to support regulatory decisions [14,15]. The Canadian HTA agency - Canadian Agency for Drugs and Technologies in Health (CADTH), has released a draft RWE guidance for public consultations [16]. These documents form foundations for greater use of RWE in regulatory and reimbursement decision-making. Moreover, there is an increase in sponsorship by the pharmaceutical industry of real-world, long-term safety studies [17].

In the European Union (EU) the European Medicines Agency (EMA) and European medicines regulatory network have established the Data Analysis and Real World Interrogation Network (DARWIN EU) [18]. This data network will pull together medical information collected in routine practice from all EU countries. Its primary aim would be to inform the European regulatory decision-making process.

Other applications of RWD of interest to the wider scientific community include clinical trial tokenisation. Tokenisation enables to anonymously link multiple data sets providing comprehensive view of the patient journey while minimising risk of re-identification [19]. It is hoped to supplement clinical trials with data gathered in routine practice informing about trial participants' health care service utilisation before, during and after the clinical trial formal follow-up period.

For years, regulators, patient advocates and health organisations have been postulating greater patient centricity in drug development and medical research. There have been numerous initiatives to put patients at the centre of the life science research and development processes. The US 21st Century Cures Act [20] addressed the need for more efficient delivery of treatments improving patient outcomes. One of the vehicles for greater patient centricity across the drug development lifecycle is patient-reported outcomes (PROs). PROs (see Box 1) – direct reports about patients' health status without interpretation by a clinician or anyone else – are utilised at various stages of medical product development [21]. Until now, PROs have been mainly used in clinical trials [22,23]. PROs are also increasingly utilised in routine medical practice to inform healthcare decision-making at the individual level [24,25]. They have been shown to improve the quality of care and support shared clinical decision-making [26]. Moreover, numerous studies have demonstrated the positive impact of PRO use on patient satisfaction, health outcomes, patient-provider communication and disease management [27–30]. Apart from being a useful tool in routine medical practice, PROs play an increasingly important role in regulatory and reimbursement decision-making, can facilitate healthcare quality improvement and inform decisions about financing healthcare services [31–33].

Despite this rapid development in the field, there is still a lack of widely accepted standards and best practices for utilising PROs in real-world studies [34]. Several guidelines on the implementation of PROs exist, but they mainly focus on randomised clinical trials (RCTs) or clinical practice [24,25,35–44]. PRO guidance specific to the RWE context is fragmented and there is a lack of international guidelines [34]. The absence of universally accepted standards for using PROs in RWE generation is deemed a key factor for its underuse. A recent analysis of the clinicaltrials.gov database shows that PROs are underutilised in phase IV clinical studies compared to earlier stages of clinical research [45]. In addition to the lack of guidelines, triallists and other experts may experience other barriers to the use of PROs in RWE generation. A recent survey by the Professional Society for Health Economics and Outcomes Research (ISPOR)

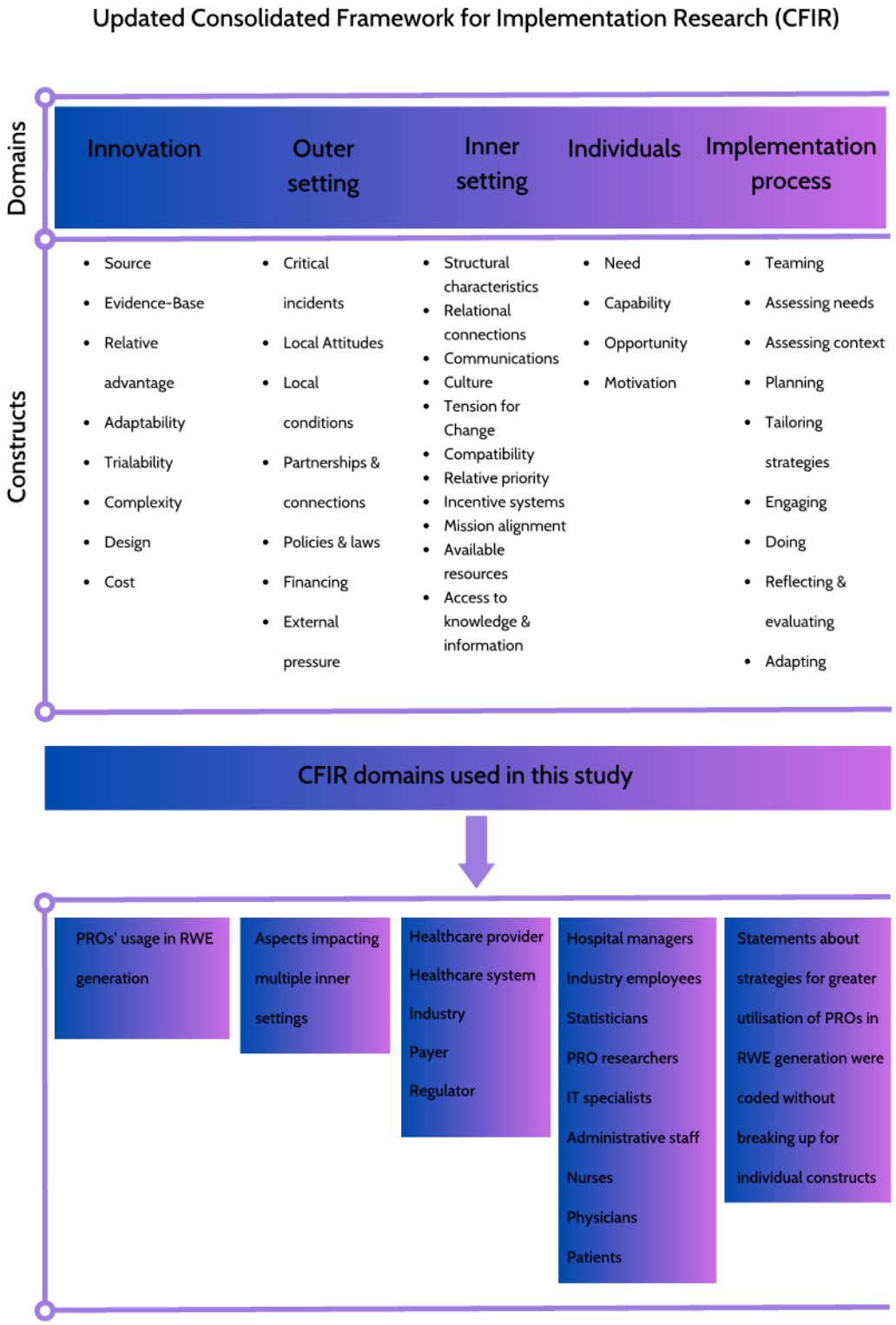

Fig. 1. CFIR conceptual framework (adapted from Damschroder et al.)
Legend: CFIR, Consolidated Framework for Implementation Research; IT, information technology; PRO, patient-reported outcomes; RWE, real-world evidence.

identified lack of transparency about the design of real-world studies and challenges with the analysis of PRO data collected in these studies, including approaches to dealing with missing data [46].

This qualitative study explores the stakeholders' perspectives on using PROs in a real-world setting. Specific objectives were to: (1) establish the current practice in the use of PROs in RWE generation, (2) identify stakeholders' needs for use of PROs in real-world studies, (3) explore the perspectives of different stakeholders on the current and future practice of PRO use in RWE generation and (4) better understand barriers and facilitators for the use of PROs in real-world studies.

2. Materials and methods

The study and all study materials were approved by the Science, Technology, Engineering and Mathematics Ethical Review Committee at the University of Birmingham (Reference number: ERN_21–1240).

2.1. Methodology and methods

Qualitative methodology was selected for this study, as it allows better understanding of participants' believes, behaviours, experiences and attitudes [47–49]. Semi-structured interviews were deemed an appropriate research method due to their ability to retain comparability between interviews. In addition, their relative flexibility allows for collecting in-depth data [47,50–52].

2.2. Participant selection

Participants were purposively recruited using two approaches. We approached leaders in PRO and RWE areas, who were identified during a previously conducted literature review [34]. Participants were also recruited utilising the existing University of Birmingham Centre for Patient Reported Outcome Research's (CPROR) networks and contacts. Invitation emails, participant information, and consent forms were sent out to the potential participants. Interviews were subsequently scheduled with those who accepted our invitations and provided written informed consent. Two types of participants have been distinguished: patient experts [53,54] (patients and patient advocates - individuals associated with patient groups or organisations that represent and support patients and their families living with a specific condition) and other experts (academic researchers, regulators, payers and industry experts). Patient experts were offered £20 vouchers as reimbursement for their participation.

2.3. Data collection

Semi-structured in-depth interviews were conducted using topic guides prepared by the study team. Two separate topic guides were developed – one for patient experts (Appendix 1) and one for other experts (Appendix 2). Topic guides were formulated based on the findings from previously published systematic reviews and discussions within the research team [34,45].

Interviews were conducted between February and October 2022 and held online using Zoom™. Conversations lasted between 40 and 90 min. Two pilot interviews were conducted by KM and observed by a second researcher (CM) to check the effectiveness of the topic guide in eliciting the required information. All conversations were audio-recorded and transcribed verbatim using Zoom's built-in features. Transcripts were then checked for correctness and amended where necessary by KM.

2.4. Data analysis

2.4.1. Analytical framework

The updated Consolidated Framework for Implementation Research (CFIR) underpinned data collection and analysis (Fig. 1) [55]. The CFIR framework is a commonly used data extraction tool for the characterisation of the determinants of effective implementation of innovations in healthcare [56]. It provides a comprehensive framework of constructs, which can be consistently used for systematic analysis and organisation of diverse data.

The CFIR framework consists of five domains: (I) Innovation, (II) Outer setting, (III) Inner setting, (IV) Individuals and (V) Implementation process. We used the CFIR to increase the richness of our data analysis. However, not all of the constructs were applicable to our data and so were not used for analysis and presentation of findings.

2.4.2. Coding process and analysis

Two coders were involved in this work: KM coded all transcripts, and CM coded a randomly selected sample of four interview transcripts (17%). CM is a highly experienced qualitative researcher, who leads and teaches qualitative research methods courses. KM completed a qualitative research methods module for postgraduate students at the University of Birmingham before approaching this work. Both coders initially worked independently. Subsequently, they compared and discussed codes assigned to statements of individual participants. Discrepancies were discussed by the two researchers and consensus was achieved. Interview transcripts were coded using QSR NVivo 20 software [57]. A coding framework drawing on the updated CFIR [55] was used to analyse transcripts deductively. Further new constructs (five within "Inner settings" and nine within "Individuals" domains) were added in through data engagement and the analytical process.

2.5. Investigator triangulation

Preliminary findings of the qualitative analysis were presented to the patient partner (RW) and an industry professional with hands-on experience in setting up real-world studies (CB). They reflected on the data, discussed and provided their interpretations of the key themes identified [58–60]. Their contributions were incorporated into the results and discussion presented in this manuscript. Investigator triangulation was conducted to decrease the researcher's influence on the interpretation of gathered data, diversify the interpretation by using different perspectives and enhance the credibility of findings [58].

3. Results

3.1. Participants

Twenty-three semi-structured in-depth interviews were conducted as part of this study. Seven patient experts and sixteen academic researchers, regulators, payers, and industry experts consented. Characteristics of interview participants are summarised in Table 1.

3.2. Key themes

Our analysis identified themes which are presented according to the updated CFIR [55] domains. These themes and illustrative quotations are presented in Appendix 3.

Not all the updated CFIR constructs were relevant to our study, and only those applicable are included in the comprehensive results table (Appendix 3). This study defined innovation of interest as "PROs' usage in RWE generation". Five "Inner settings" were identified and described, including: "Healthcare provider", "Healthcare system", "Industry", "Payer" and "Regulator". Additionally, roles sub-domains under the "Individuals" domain was altered with stakeholders applicable to our topic (hospital managers, industry employees, statisticians, PRO researchers, information technology (IT) specialists, administrative staff, nurses, physicians, and patients). Moreover, we did not distinguish individual constructs under the "Implementation process" domain as its collateral constructs were deemed not applicable to the collected data.

The remaining of the results section describes key themes, formed by data captured in multiple domains of the updated CFIR (Fig. 2). Those themes compose the most important study findings and addresses following issues:

- sources of RWD,
- value of PROs,
- data collection as part of routine care,
- prospective data collection,
- increase in the use of PROs in routine care,
- facilitating prospective real-world studies,
- patient engagement,
- instrument design, and
- good practices dissemination.

3.3. Sources of RWD[1]

There was no agreement about the universal definition of RWD between participants (quote #37). Less than half particiapnts, mainly those with a background in academia, used a narrow definition of RWD. They considered RWD as data captured routinely as part of claims databases or electronic health records (EHRs) only. In their opinion, prospective data collection conducted as part of the study with an *à priori* research question does not fulfil the definition of RWD (quotes #39 and #40). In contrast, others (mainly industry or consultancy employees, payers and regulators) used a more inclusive RWD definition. They referred to the spectrum of real-world data sources: registries, patient surveys, observational studies and pragmatic trials.

Participants with a more conservative view on sources of RWD pointed out that participation in a study with prospective data collection has to be preceded by obtaining patient consent (quote #41). They saw selection bias imposed by the requirement of obtaining patients' informed consent as a threat to the generalisability of study findings (quote #38). Moreover, they argued that the characteristics of individuals who agree to participate in studies tend to differ from those of the general population (quote #57). Thus, data collected prospectively should not be characterised as a "real-world".

Differences in the perception of RWD sources have implications for recommendations given by participants on advancing the field. Participants who limited their definition of RWD to data collected primarily in routine care and then re-used for research, mainly focused on barriers hampering routine PRO data collection. They believed that a lack of routine PRO data collection is the main issue which needs to be addressed in the first place, and this was seen a necessary condition to advance the field (#quote 223). On the other hand, participants who adopted a broader RWE definition (quote #42) allow, at minimum, for prospective data collection, e.g.,

[1] This subsection contains data grouped under the following CFIR constructs: Innovation domain (Innovation complexity), Outer setting domain (Policies & Laws), Implementation process domain.

Table 1
Characteristics of participants.

	Patient experts (N = 7)	Other experts (N = 16)
Country		
European Union	–	3
Canada	–	3
United Kingdom	7	4
United States	–	6
Role		
Regulator	–	5
Academic researcher	–	7
Payer	–	1
Industry expert	–	3
Patient	5	–
Patient advocate	2	–
Gender		
Male	5	6
Female	2	10

supplementing data captured in EHRs. Their recommendations were more wide-reaching and not limited to operational barriers to data collection in routine care. They commented on challenges associated with running prospective real-world studies and limited acceptance of evidence generated in this way due to a lack of widely accepted standards and requirements (quote #108).

3.4. Value of PROs[2]

Almost all participants acknowledged multiple potential applications for PROs in RWE generation (quote #7). Efficiencies associated with collecting PRO data were realised through their use to inform individual patient care and building up an evidence base to support decision-making processes, e.g. treatment option selection (quotes #11 and #12). It was observed that different participant types had different expectations with respect to PROs' value. Most of the patient experts saw PROs as a tool that, in the first place, can inform their care – utilising their responses for disease progression monitoring or as a vehicle for building up evidence to help other patients with similar conditions in the future to choose the most appropriate treatment method (quotes #200 and #206). Moreover, they were seen as a valuable tool for self-diagnosis and regaining power over their healthcare (#quote 18). Clinicians often saw PROs as a means to identify patients who require special attention and improve care of individual patients (quotes #19 and #181–183). All regulators and payers mentioned the potential of PROs collected in the real-world in supplementing evidence currently used to inform their decisions (quotes #73 and #152).

Nevertheless, statements from five participants pointed out that the PRO RWD field is not yet well established. Interviewees realised that it is difficult to assess how big a role PROs will play in the RWE space as we are still very early with its implementation for this purpose (quote #72). Moreover, participants with a background in regulatory and payer organisations were unsure how exactly PROs collected in the real-world setting could informed their decisions due to the lack of guidance (quote #148).

3.5. Data collection as part of routine care[3]

The primary problem perceived by the participants in this area is the lack of routine data collection in most jurisdictions (quote #97). Less than half participants highlighted that efforts need to be made to initiate data collection in selected sub-populations of interest. They noticed that appropriate infrastructure must be in place to support data collection in routine practice (quote #98). It usually requires large-scale implementation, often at the health system level (quote #78). Thus, more than half of the participants identified operational and infrastructural barriers hampering the introduction of PROs associated with a lack of appropriate IT systems, funding or integrating data collection into current workflows and practices (quotes #75, #127, #134 and #136). Some participants emphasised that the primary reason for collecting PROs is to inform routine medical practice at the individual level. PRO data are then recorded as part of EHRs and can be later re-used for research purposes (quote #40). A few participants, however, noted that PRO data are rarely collected routinely (quote #97). Additionally, concerns about the suitability of PRO instruments used to inform individual decision-making for answering specific research questions of interest were raised (quote #217) by a few participants.

[2] This subsection contains data grouped under the following CFIR constructs: Innovation domain (Innovation Relative Advantage, Innovation complexity), Individuals domain (Patients(Motivation), Physicians(Motivation)), Inner settings domain(Regulator(Work infrastructure), Payer (Compatibility)).

[3] This subsection contains data grouped under the following CFIR constructs: Innovation domain (Innovation cost, Innovation complexity), Outer setting domain (Local conditions), Inner settings domain (Healthcare provider (IT infrastructure, Funding).

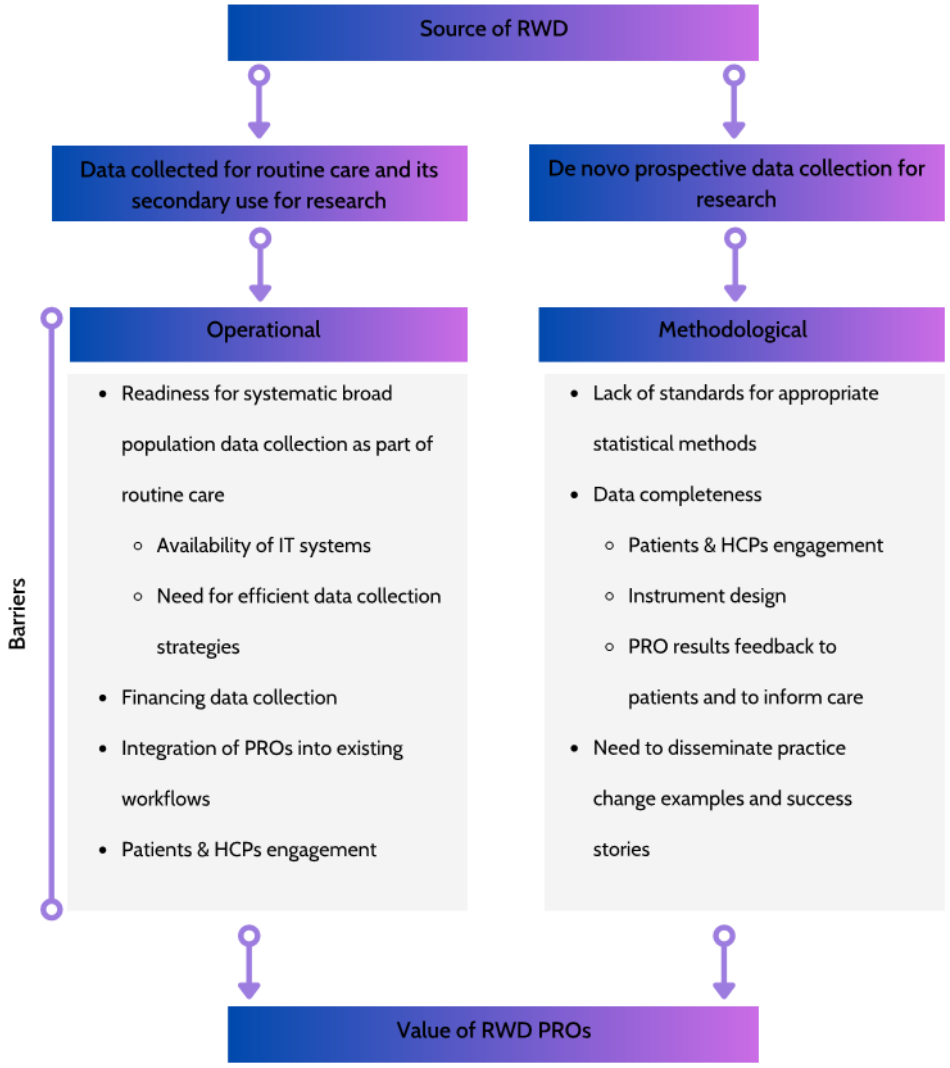

Fig. 2. Key study findings: modes of PRO data collection, barriers for its full implementation and impact on their perceived value
Legend: HCPs, healthcare professionals; IT, information technology; PROs, patient-reported outcomes; RWD, real-world data.

3.6. Prospective data collection[4]

The majority of participants admitted that despite increasing interest in their use, PRO data are still rarely collected to inform routine care (quote #133). Even if they are, it is not clear whether PRO instruments selected primarily to inform care at the individual level would be able to answer the research question pertaining to RWE generation. Industry and consultancy employees described that usually, EHRs do not hold all necessary information (e.g., PRO data not collected or unsuitable PRO instrument used, timing of assessments does not allow to address research question, missing data), and most of the time, some form of prospective data collection is required. A few participants acknowledged that in the case of prospective data collection, there is no need for a lengthy and challenging process of delivering infrastructural change at the health system level to ensure that appropriate tools for PRO data collection are in place. Instead, the study sponsor is responsible for recruiting sites eager to participate in the research project and finances the site(s) for data collection. In that case, sponsors also coordinate the implementation of necessary IT tools (quotes #80 and #118). Participants noticed that PRO responses obtained in this way might (quote #11) or might not (quote #128) be fed back to the clinicians and be actively used in the care delivery for study participants.

3.7. Increase in the use of PROs in routine care[5]

Several barriers that must be addressed to allow for the more common use of PROs in routine medical practice were reported. First, large-scale infrastructure changes are required (quotes#134 and #137). Less than half participants noted that policymakers could mandate or incentivise PRO data collection (quotes #111 and #112). The public sector was also often mentioned to be involved in financing data collection to some extent (quotes #111, #115 and #116). Additionally, it was often mentioned that the successful implementation of PROs into clinical workflows requires a change of behaviour from healthcare professionals (HCPs) (quote #130). Their buy-in and actual utilisation of PROs, e.g. by discussing patient responses, impacts patients' willingness to provide data (quote #176). Several approaches can be taken to encourage patients to provide data, including educating them about the value of PROs and informing them about the purpose of data collection (quotes #201, #205 and #219).

A few participants postulated that the successful implementation of PROs into clinical practice should be facilitated by creating an ecosystem of highly engaged HCPs – champions, who help demonstrate the value of PROs to their peers (quote #184). More than a half participants believed that HCPs must acknowledge the importance of using PROs in routine care (quote #180) to allow for its successful use in clinical practice. Their positive attitude should keep patients motivated and help sustain their long-term reporting (quote #196). Moreover, around a quater of participants mentioned that realising the benefits of PROs in individual's care should, on the other hand, motivate patients to report (quote #206). Data gathered in this way can be then re-used in RWE generation (quote #222). According to less than half participants, this evidence can be used to better inform the care of future patients struggling with similar conditions (quote #12). Almost of participants realised that making it happen is not easy and straightforward (quote #71). They noticed that successful implementation strongly depends on the involvement of health institutions, which are often rigid, and getting them on board might be tedious (quote #220). On the other hand, a few participants argued that guidelines and standards for PRO use in routine care are already available [24,25,44,61,62], which should enhance the use of PROs in routine care and indirectly accelerate PROs implementation for RWE generation as well.

3.8. Facilitating prospective real-world studies[6]

A commonly mentioned barrier hampering the broader use of prospective real-world studies is the lack of guidelines and well-established standards for their implementation (quotes #89–90 and #108). Success stories demonstrating the added value of PROs collected in real-world settings are needed (quote #227), according to majority of study participants. They argued that practice change resulting from these type of studies could help convince a wider scientific audience about their usefulness (quotes #92 and #226). Less than half participants added that lessons learned along successful PRO implementations should be reflected in emerging good practices e.g. decision-makers' guidelines informing how RWE can influence their decisions (quotes #109–110 and #225). Majority of industry and consultancy employees stated that running prospective studies seems a more manageable task, which does not entail changes at the health system level (quote #80). A few participants reported that the industry is interested in sponsoring this type of evidence generation, and there is a growing number of successful completed studies of this design (quote #118). At the same time companies struggle to use this evidence in regulatory or reimbursement processes (quote #110). They noticed that the value of this type of evidence was not fully understood yet, and thus decision-makers are reluctant to accept it (quotes #88–92).

[4] This subsection contains data grouped under the following CFIR constructs: Innovation domain (Innovative relative advantage), Outer setting domain (Financing), Inner settings domain (Healthcare provider(Compatibility, IT infrastructure)).

[5] This subsection contains data grouped under the following CFIR constructs: Innovation domain (Innovation Relative Advantage, Innovation Complexity), Outer setting domain (Policies & Laws, Financing), Inner settings domain (Healthcare provider(Funding, IT infrastructure, Work infrastructure)), Individuals domain (Physicians(Opportunity, Motivation), Patients(Motivation)), Implementation process domain.

[6] This subsection contains data grouped under the following CFIR constructs: Innovation domain (Innovation cost), Outer setting domain (Local attitudes, Policies & laws, Financing), Implementation process domain.

3.9. Patient engagement[7]

Issues around patient engagement and burden apply to both primary and secondary use of PRO data and were frequently mentioned by participants. Majority of participants emphasised that patients should be engaged at every step of the study (quote #201). They are vital in setting up the research, selecting PRO instruments and proselytising participation (quote #204). A few participants stated that PRO instruments used for data collection must be relevant to the participants' health states to facilitate long-term patient retention (quotes #189–191). Participants shared several recommendations that should be used when designing and implementing studies. Firstly, the time needed to complete questionnaires and the frequency of data provision should be considered as it impacts patients' burden and willingness to provide data (quotes #188 and #195). Secondly, in general patients are eager to share their experiences and provide the study with their data (quotes #197–199). Besides informing their care, PRO data provision is often motivated altruistically (quotes #206 and #200). Patient experts often mentioned that the awareness of contributing to the ongoing research and helping patients with similar health problems is an important motivator for providing their data. Participants pointed out that patients should be informed about the purpose of data collection and study progress (quote #201). Patient experts frequently mentioned that receiving feedback with study results is a significant incentive to continue providing data (quote #205). They also mentioned that updating them about the progress of the study, is often perceived as a form of thanking participants for their involvement in the research. Moreover, majority of participants stressed that it is crucial to use collected data and act upon them if made available to the health teams (quote #50).

3.10. Instrument design, selection and administration[8]

Patient experts shared considerations for designing and selecting PRO instruments in the real-world setting. Firstly, tools for data collection should be compatible with different operating systems and device types (laptop, tablet, mobile) (quote #211). Secondly, patient-reported outcome measures (PROMs) should have an attractive and easy-to-follow layout (quote #212). Patient experts also often pointed out that questions should be simple, free from spelling mistakes and without extensive use of abbreviations. They also often mentioned that electronic data capture should be supported by automated reminders, as it helps keep participants engaged and reduces the number of missing measurements (quote #215).

3.11. Good practices dissemination[9]

Less than half of the participants highlighted that educating stakeholders across the board is essential for successful implementation of PROs in RWE generation. Patients, regulators, payers and industry workers should be informed about the value of PROs in the real-world setting and the benefits associated with different use cases of PROs (quote #219). Participants frequently mentioned that international scientific societies can be an excellent platform to share experiences and emerging good practices for running real-world studies. A few participants argued that examples of methodologically robust studies leading to practice change should convince regulators and payer that their decisions can be made in greater extend based on RWE (quotes #226–227). As reported by a few participants this should ultimately lead to development of guidance and setting up acceptable level of evidence for different use cases for regulatory and reimbursement decision-making.

4. Discussion

This study revealed the attitudes of stakeholders towards using PROs in the RWE generation. Participants listed multiple potential applications for PROs in a real-world setting. Nevertheless, numerous barriers hampering the broader use of PROs were also identified. Mixed opinions about the value of PROs in RWE generation were present, indicating that the field is still in the early stages of development.

Barriers can be grouped as operational and methodological challenges, and they must be addressed to advance the field to exercise the full benefits of PROs in RWE generation. Operational challenges associated with PRO data collection in routine care include: setting up systems for collecting PRO data from broad populations as part of their routine care, implementing efficient data collection strategies, ensuring appropriate financing is in place, building up IT infrastructure, and integrating data collection into existing workflows. Methodological issues mentioned were often focused on strategies for dealing with missing data. Efforts should be made to maximise the completeness of the gathered data sets (participant and HCPs engagement, result feedback to patients, etc.). Statistical methods for dealing with missing data exist and can be successfully carried over from the clinical trial environment, but guidance is needed to indicate which methods are acceptable in particular use cases. The need for guidance for more appropriate use of Clinical Outcome Assessments (COAs), including PROs, to meet challenges present in real-world studies was also recently mentioned by Rylands and colleagues [46]. They acknowledged that robust study design to guide selection, analysis, interpretation and integration of COAs is of critical importance for generating high-quality, fit-for-purpose and meaningful RWE, which is in line with our findings. Thus,

[7] This subsection contains data grouped under the following CFIR constructs: Innovation domain (Innovation Complexity), Individuals domain (Patients (Motivation, Capability, Opportunity)).

[8] This subsection contains data grouped under the following CFIR constructs: Implementation process domain.

[9] This subsection contains data grouped under the following CFIR constructs: Implementation process domain.

standards should be set to avoid confusion about the analytical approaches used. Widely accepted methodological standards and data collection practices should be reflected in the emerging good practices.

The lack of consensus about the definition of RWE was also reported in a study where regulators and payers were interviewed [63]. The lack of agreement on the study setting constituting RWE hampers guidance development and advancing the field. Ambiguity around RWE term can also lead to misunderstandings between different healthcare stakeholders [63]. Calvert et al. [64] summarised priorities which need to be addressed to allow for greater inclusion of PROs in RWE. Challenges reported by participants of this study overlap to great extent with those priorities.

Our findings identified two areas of focus to facilitate utilisation of PROs in real-world studies. The first is to address operational challenges associated with collecting routine PRO data to inform care delivery at the individual level. The second is to focus on addressing methodological and other challenges related to studies collecting prospective *de novo* data in real-world setting.

Another frequently mentioned issue which needs to be addressed is how to fund PRO data collection. Multiple possible funding entities were mentioned by participants – government, payers, pharma companies and healthcare providers. Several models of financing PRO data collection are possible and should be explored in future research. The collection of PROs as part of managed access programs (as described in glossary, Box 1) poses a promising opportunity for its broader utilisation. PROs might provide a valuable source of information for re-evaluating a drug when the initial reimbursement decision was burdened with uncertainties around meaningful endpoints to patients. Additionally, post-authorisation safety and tolerability studies were highlighted as those with a potential for substantial PRO usage in a real-world setting.

Further research is needed to determine the value of PROs collected in real-world settings for various use cases. Practice-changing studies are required to demonstrate the full potential of PROs. Efforts of regulators, payers and the broader scientific community are needed to guide how this type of data should be collected, analysed, interpreted and integrated to provide robust answers to questions asked by different stakeholders. Most likely future standards for using this type of data will depend on the study setting and sources of RWD. Thus, recommendations may need to be tailored to specific use cases of PROs collected in a real-world environment.

5. Strengths

Our study recruited participants representing various roles, organisation types and viewpoints. Due to that, we were able to gather a rich data set suitable for meaningful qualitative analysis. Different perspectives and opinions were presented, allowing for identifying areas lacking agreement where additional research is needed.

6. Limitations

Given the size of the study sample, the findings may not represent the views of all stakeholder group. However, the qualitative nature provides the opportunity to explore in depth the views of participants in a manner that would not be possible using quantitative methods such as surveys. Most of the individuals recruited for the study have a keen interest in PROs or are professionally engaged in RWE. This makes them valuable and knowledgeable sources of information about issues in the scope of this research. But it can introduce bias as our interviewees might present a more favourable outlook on PROs in the RWE generation than the broader clinical research community. Furthermore, patient experts participating in this study were recruited solely in the UK, which might limit the generalisation of our findings in other geographic locations.

7. Conclusions

The use of PROs in RWE generation is not well established yet. Several opportunities and challenges were identified regarding the broader use of PROs in RWE research. A mixed level of confidence about the value of PROs collected in a real-world setting is present among participants. Barriers hampering the full implementation of PROs in RWE generation can be grouped as operational and methodological. The needs of various stakeholder groups (including patients, HCPs, regulators, payers, and industry) should be considered when implementing PROs. Setting good practices for PRO data collection, analysis, and use in the real-world would help to maximise its benefits.

Ethics statement

The study and all study materials were approved by the Science, Technology, Engineering and Mathematics Ethical Review Committee at the University of Birmingham (Reference number: ERN_21–1240). Informed consent was obtained from all study participants.

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Contributorship

Konrad Maruszczyk, Christel McMullan: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Olalekan Lee Aiyegbusi, Thomas Keeley, Melanie J Calvert: Conceived and designed the experiments, Contributed reagents, materials, analysis tools or data; Wrote the paper.

Roger Wilson, Philip Collis, Catherine Bottomley: Analyzed and interpreted the data; Wrote the paper.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Konrad Maruszczyk reports financial support was provided by GSK plc. Melanie Calvert reports financial support was provided by GSK plc. Christel McMullan reports financial support was provided by GSK plc. Olalekan Lee Aiyegbusi reports financial support was provided by GSK plc. Melanie Calvert reports a relationship with NIHR Birmingham Biomedical Research Centre that includes: funding grants. Melanie Calvert reports a relationship with Health Data Research UK that includes: funding grants. Melanie Calvert reports a relationship with Innovate UK that includes: funding grants. Melanie Calvert reports a relationship with Macmillan Cancer Support that includes: funding grants. Melanie Calvert reports a relationship with GSK plc that includes: consulting or advisory and funding grants. Melanie Calvert reports a relationship with UCB Pharma SA that includes: funding grants. Melanie Calvert reports a relationship with Research England that includes: funding grants. Melanie Calvert reports a relationship with European Commission and EFPIA that includes: funding grants. Melanie Calvert reports a relationship with Brain Tumor Charity that includes: funding grants. Melanie Calvert reports a relationship with Gilead Sciences Inc that includes: funding grants. Melanie Calvert reports a relationship with Janssen Pharmaceuticals Inc that includes: funding grants. Melanie Calvert reports a relationship with National Institute for Health and Care Research that includes: funding grants. Melanie Calvert reports a relationship with UK Research and Innovation that includes: funding grants. Melanie Calvert reports a relationship with Aparito that includes: consulting or advisory. Melanie Calvert reports a relationship with CIS Oncology that includes: consulting or advisory. Melanie Calvert reports a relationship with Takeda UK Ltd that includes: consulting or advisory. Melanie Calvert reports a relationship with Merck & Co Inc that includes: consulting or advisory. Melanie Calvert reports a relationship with Daiichi Sankyo Inc that includes: consulting or advisory. Melanie Calvert reports a relationship with Glaukos Corporation that includes: consulting or advisory. Melanie Calvert reports a relationship with Patient-Centered Outcomes Research Institute that includes: consulting or advisory. Melanie Calvert reports a relationship with Genentech that includes: consulting or advisory. Melanie Calvert reports a relationship with Vertex that includes: consulting or advisory. Melanie Calvert reports a relationship with Icon plc that includes: consulting or advisory. Melanie Calvert reports a relationship with University of Maastricht that includes: speaking and lecture fees. Melanie Calvert reports a relationship with Cochrane Portugal that includes: speaking and lecture fees. Melanie Calvert reports a relationship with South-Eastern Norway Regional Health Authority that includes: paid expert testimony. Melanie Calvert reports a relationship with Singapore National Medical Research Council that includes: paid expert testimony. Melanie Calvert reports a relationship with PROTEUS Consortium that includes: board membership. Catherine Bottomley reports a relationship with Vitaccess Limited that includes: employment. Olalekan Lee Aiyegbusi reports a relationship with GSK plc that includes: consulting or advisory and funding grants. Olalekan Lee Aiyegbusi1 reports a relationship with Merck & Co Inc that includes: consulting or advisory. Christel McMullan reports a relationship with National Institute for Health and Care Research that includes: funding grants. Christel McMullan reports a relationship with CIS Oncology that includes: funding grants. Christel McMullan reports a relationship with Aparito that includes: consulting or advisory. Thomas Keeley reports a relationship with GSK plc that includes: employment and equity or stocks.

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Appendices. Supplementary data

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Chapter 6: Discussion

6.1 Summary of findings

This doctoral research aimed to characterise the use of PROs in RWE generation and identify challenges and opportunities to implement RW-PROs successfully. A mixed-method approach was followed to achieve these goals. Both qualitative and quantitative methods were used to address the research question.

Firstly, a systematic review was conducted to identify available guidance facilitating the collection and use of RW-PROs for regulatory, reimbursement and health policy decision-making (Chapter 3).[1] Although the review revealed that some level of RW-PRO guidance is available, it lacks cohesion. Available publications focused only on selected aspects of RW-PRO use or specific patient sub-populations (e.g. safety reporting or elderly patients). No comprehensive guidelines holistically supported the use of PROs in RWE generation. Moreover, no international guidelines directly addressing the application of RW-PROs were found.

A quantitative analysis of the ClinicalTrials.gov database followed. Records of clinical trials were searched to characterise the uptake of PROMs among RW studies. An automated computer algorithm was executed to identify phase IV clinical trials assessing PROs as one of the endpoints (Chapter 4). Among 27,976 phase IV clinical trials registered on Clinicaltrials.gov between 1999 and July 2021, 21% incorporated PROMs.[2] Notably, a continuous rise in PROM utilisation emerged since 2019, exceeding 25% of phase IV studies assessing PROMs in 2021. PROMs mainly served as secondary endpoints within these trials. The analysis revealed that phase IV trials in four specific areas - "Behaviors and Mental Disorders," "Ear, Nose, and Throat Diseases," "Nervous

System Diseases," and "Respiratory Tract (Lung and Bronchial) Diseases" - saw the highest utilisation of PROMs. The five most prominent PROMs included Quality of Life (umbrella term encompassing various PROMs), 36-item Short Form Health Survey (SF-36)[3], EQ-5D[4], Montgomery-Asberg Depression Rating Scale[5], and the Western Ontario and McMaster Universities Arthritis Index[6].

Qualitative research, which explored in-depth perspectives of international stakeholders about challenges and opportunities for using RW-PROs, is presented in Chapter 5.[7] Participants were recruited among patients and professionals in various healthcare system roles. Their views and opinions were utilised to identify strategies for enhancing the uptake of PROs in the RWE generation.

While participants acknowledged the potential of PROs, they also articulated that capturing patient perspectives through collecting and utilising PRO data in RWE remains challenging. RW-PROs are collected in settings which differ from highly controlled clinical trial environments, where their use has been well established over the years. Numerous obstacles related to data collection and analysis, e.g. patient recruitment, informed consent, data collection time points, and higher data missingness, must be addressed to benefit fully from the RW-PROs.

Study participants highlighted the need for further development of methods and more widespread collection of PRO data outside the research setting. Notably, varying levels of confidence in the value of RW-PROs were visible. Clearly, the use of PROs collected in real world settings is still a developing field. It is yet to be seen to what extent RW-PROs will be able to support manufacturers' claims in regulatory and reimbursement processes.

Participants reiterated that practice changing examples are needed to demonstrate the value of RW-PROs.

6.2 Interpretation and implications of findings

6.2.1 Reasons behind lower utilisation of PROs among RW studies

As shown in Chapter 4, 21% of phase IV trials utilised PROMs.[2] This indicates that PROMs are used less frequently in phase IV trials than in earlier phases of clinical research. Previous work by Vodicka et al.[8] summarising the utilisation of PROMs among all phases of clinical trials (without restricting to phase IV studies only) revealed that 27% of studies between 2007 and 2013 collected PRO data. The limited widespread adoption of PROMs in phase IV trials was unclear. Potentially, it was due to heightened challenges in collecting PRO data in RW settings and a lack of consensus on optimal data collection and analysis methods. Integrating PROs necessitates added responsibilities for healthcare professionals, adjustments to clinical protocols, and incurs additional expenses. Moreover, remote PRO collection, increasingly used in RW studies, mainly relies on patient engagement to complete the measures over the long term, posing potential challenges. These examples illustrate just a fraction of the obstacles hindering the full integration of PROMs in the RW contexts and were further investigated as part of qualitative interviews included in this PhD work.

Speculations about reasons for lower utilisation of PROs among RW studies were confirmed by some of the findings of qualitative study as presented in Chapter 5. Two key barrier types hampering the implementation of PROs for RWE generation were identified: operational and methodological. Operational challenges hinder the collection of RW-PRO

data in routine clinical practice. They relate to the readiness of appropriate IT infrastructure, availability of dedicated resources, or implementation of PROs into existing workflows.

On the other hand, methodological barriers relate to the robustness and interpretability of RW-PRO data, of which there is a dearth of guidance available to support researchers in designing RW studies. The lack of widely accepted data collection and analysis standards hampers the acceptance of this type of evidence in decision-making processes. Addressing these barriers is crucial to unlock the full potential of PROs in RWE studies.

Although study participants expressed multiple prospects of RW-PROs, the true value of PROs in RWE generation is yet to be seen. Some participants pointed out that the RW-PRO field is not yet well established. As the utilisation of RW-PROs is still in its early days, interviewees realised it is difficult to assess if PROs will play a significant role in the RWE space. For example, concerns exist about the extent to which healthcare systems can scale up the utilisation of PROs to exercise their benefits at the population level as part of routine care delivery. Previous studies have demonstrated that using PROs in routine care can improve patient communication and satisfaction and positively impact health outcomes.[9-11] Unfortunately, it remains unclear how feasible it is to extrapolate PROs' benefits at the system level. Proliferating PRO use within routine care requires devoting valuable resources. They are needed to accommodate data collection activities and efforts to utilise gathered information. This includes money, staff, and time, which will not be spent elsewhere within the healthcare systems. Thus, the added value of RW-PRO initiatives must be demonstrated to decisionmakers to allow such resource allocation.

Moreover, this PhD has demonstrated insufficient understanding within the scientific community of how PROs collected in RW settings can inform decision-making processes. It remains unclear what types of claims can be supported with RW-PROs. Regulatory and reimbursement decisions require robust data to be used in these processes. Currently, there is a lack of confidence about the level of scrutiny that needs to be put into RW-PRO data collection and analysis to generate regulatory-grade information. The lack of standardised approaches to PRO use in RWE aligns with the scientific community's reported hesitancy in leveraging this data for decision-making. Stakeholder interviews revealed that methodological challenges and the absence of widely accepted standards hinder the full implementation of RW-PROs and discourage investment in running such studies.

The use of RW-PRO data for regulatory label claims is in its early stages, which explains the hesitation to fully embrace it. It is possible to refer to the experience with clinical trial PRO data for context. The FDA issued specific guidance on using PRO data in regulations in 2009.[12] Several studies have been conducted since then, highlighting progress in incorporating patient perspectives into regulatory decisions.[13-15] However, significant room for improvement remains.[15]

For example, a study of oncology drugs approved between 2010 and 2020 found that few labels included PRO claims, and those offered limited information.[15] Additionally, the language used was often not patient-friendly, and there was a potential bias towards positive outcomes.[15] Inconsistencies were also observed between US FDA and EMA

labelling regarding PROs.[15] These findings suggest that the current use of PROs for oncology drug labels is suboptimal, and greater global harmonisation is needed.[15]

The experience with clinical trial PRO data suggests that building confidence and establishing best practices takes time and requires a lot of convincing. Despite existing guidance on using PROs in regulatory decisions (see section 1.2.7.2) and over a decade of experience there is still space for improvement in the uptake of PROs in health research.

Participants of interviews presented in Chapter 5 considered the RW-PROs field as underdeveloped. The limited availability of standards supporting the collection and use of RW-PROs was confirmed by the results of the systematic review presented in Chapter 3. It highlights the fragmented nature of current guidelines, with no international consensus specifically addressing PROs in RWE generation. This fragmentation reflects the diverse data sources and heterogeneous study designs inherent to RWE studies themselves. To address this gap, future RW-PRO guidelines should be adapted to specific contexts of PRO use. Furthermore, broad stakeholder engagement is crucial, including researchers, HCPs, patient groups, regulators, payers, and industry.

The field of RWE is undergoing rapid advancements. Since the completion of the SLR, several regulatory bodies and payers have released guidance documents (e.g., [16-20]) specifically focused on utilising RWE to inform decision-making processes. While these documents don't directly address PROs, they offer valuable general principles for using various RWD sources and generating robust RWE. These principles can be informative when considering RW-PROs as well.

One particularly relevant document is the preliminary guidance for PRO collection within registries.[21] Though specific to PROs collected in a particular type of RWD study, these recommendations offer valuable insights for utilising PROs outside of research settings. The recommendations outlined in this publication can likely be adapted for use in other types of RWD studies involving RW-PROs.

Another valuable resource is the PROTEUS Clinical Practice PRO Guide.[22] This publication consists of summaries of various PROTEUS Consortium resources on practical considerations for PRO data collection and its use in informing routine care delivery. While evidence generation is not the primary focus of this resource, the insights gained regarding data collection strategies can be successfully applied for RWE generation purposes using RW-PROs. In essence, these newly available guidance documents provide a framework for researchers to leverage RW-PRO data for RWE generation, even though they were not explicitly designed for this purpose.

6.2.2 RW-PROs are gaining traction

The increasing utilisation of PROMs in phase IV studies since 2019, illustrated in Chapter 4, is in line with testimonies collected as part of the qualitative study. Participants of interviews presented in Chapter 5 acknowledged the potential of RW-PROs and reiterated that incorporating RW-PROs can provide a more holistic assessment of patient health. Historically, RW studies have mainly investigated data on healthcare resource utilisation, clinical events, and results of various medical tests. Thus, the inclusion of RW-PRO enables patients' perspectives to be considered for evaluation of the true impact of treatments.

Stakeholder interviews showed that RW-PROs can provide many potential advantages for healthcare research. They aid in gaining deeper insights into diseases and intervention experiences from the patient's viewpoint while also encompassing medical products' long-term safety and effectiveness across a wider population. By assessing interventions in RW settings, research findings can become more applicable to diverse populations, fostering inclusivity and equity. The possible benefits of RW-PROs mentioned by study participants might partially explain the gradual increase in including such outcomes in RW studies.

A steady, gradual increase in the uptake of PROs among phase IV trials, observed since 2019, aligns with previously published results, demonstrating growing interest in utilising PROs in all phases of clinical studies in the long run. One of the first analyses[23] characterising PRO utilisation from 1997 yielded 4.2% of trials assessing this endpoint. A similar percentage (4.4%) was observed by Naito et al.[24] among Japanese trials between 2000 and 2003. Another analysis[25] focusing on Clinicaltrials.gov records from 2004-2007 reported that 14% of trials used at least one PROM. The results from this PhD research (21% of phase IV trials incorporated PROMs), consistent with prior studies, affirm the increasing utilisation of PROMs in clinical investigations. Furthermore, they illustrate a parallel trend in utilising PROMs among RW studies.

6.3 Recommendations for future research

6.3.1 Guidance and standards

This thesis highlights the nascent state of PROs in the RWE generation. While the field is gaining traction, developing robust standards for RW-PRO use necessitates sustained

effort from the broader scientific community. Building expertise and knowledge through collaborative efforts is essential. Proving value of RW-PROs requires demonstrating success stories and practice-changing case studies of their use in regulatory, reimbursement, and health policy spaces.

I believe that generating such examples will be a long-term endeavour that will require substantial efforts to persuade multiple agents within the healthcare system. Gaining buy-in from various stakeholders will be essential to fully embracing the use of RW-PROs.

Regulatory and HTA bodies play a crucial role in promoting acceptance of RWE. Initiatives from these stakeholders, such as documents guiding RW-PRO collection and use, would be highly beneficial. Such guidance could establish quality standards and communicate the value of RW-PRO data. Clear standpoint of these organisations about acceptability of RW-PRO would incentivise industry investment and could mitigate risks associated with funding RWE studies.

The current scarcity of best practice guidance and success stories underscores the need for further exploration. Collaborative efforts across the scientific community are paramount to propel the field forward. Over time, broadly accepted standards for RW-PRO application are likely to emerge. Regulatory bodies and payers could then integrate these learnings into their guidance documents.

A promising initiative in this regard is the recently established “PROs in Prospective Real World Study Design ISPOR Task Force”.[26] This collaborative work is underway and will be informed by the findings of this PhD research project. The Task Force aims to identify

and describe emerging best practices for using PROs in prospective RWE studies. Such initiatives are of key importance to address the methodological challenges that need to be faced by RW researchers.

6.3.2 Stakeholder involvement

Further initiatives are needed to promote the involvement of patients, the public, and RWE end users in RW study design. Additionally, measures to improve engagement with participants in RW studies are crucial.

6.3.2.1 Enhancing patient and public involvement in RW studies

This PhD research confirmed the importance of involving patients and the public early in RW study design. Interview participants emphasised including patients at the design stage as a critical success factor. The need to co-design RW studies with patients aligns with previously published PPIE guidance documents on this topic.[27-31] The involvement of patients throughout all stages of research, including the development of grant proposals, project setup, study design, dissemination of study findings, and evaluation of PPIE, was recommended by Aiyegbusi et al.[27]

Patients' contributions at the early stage of RW study development allow them to comment on the numerous aspects of the study. Their input should be used to inform selection of appropriate recruitment strategies, PROMs selection, and well-suited modes of data collection. All these factors impact the inclusivity and equity of research and have the potential to maximise participant retention.

6.3.2.2 Enhancing patient motivation for data submission

PPIE throughout the research process has its important implications for maximising quality and quantity of collected PRO data. Incorporating a robust PPIE approach during the design and execution of the research is crucial. This could involve co-designing recruitment strategies with patient partners, focusing on retention strategies that address patient needs, developing compliance strategies through collaborative workshops or providing regular study progress updates. This fosters a sense of ownership and acknowledges the valuable contributions patients make to study design, ultimately improving participant motivation to continue providing PRO data. By prioritising patient engagement and optimising data collection methods, RWE studies can harness the power of patient reported data while minimising participant burden. This will ultimately lead to more robust and patient-centred real world evidence.[32]

This PhD research identified a critical gap in patient engagement strategies for RW studies, particularly those utilising remote PRO. As RW studies increasingly rely on patient-submitted data, maximising patient engagement and willingness to provide becomes paramount.

The study highlights the need for research to identify optimal data collection strategies that minimise respondent burden in RWE studies using remote PROs.[33] This could involve exploring innovative data capture methods, tailoring them to specific patient populations, and investigating optimal survey frequency.

Future research should rigorously evaluate various initiatives designed to motivate data submission. Developing educational strategies that inform patients about the value of

PROs in RW settings, along with the benefits associated with different PRO use cases, could significantly impact patient engagement. Implementing automated reminders for electronic data capture can be a crucial strategy for bolstering participant engagement and minimising the occurrence of missing measurements.

6.3.2.3 Mitigating challenges in the design of PRO systems utilised for multiple purposes

Consulting with end-users during PRO system design is critical for RW-PRO data collections aiming to be utilised for multiple purposes. Early consideration of potentially competing needs from various end-users can alleviate future challenges.[32] Further research is needed to explore solutions for these complexities. Achieving full integration of PROs in RWE generation necessitates collaborative efforts from various multidisciplinary stakeholders to overcome existing obstacles.

Qualitative interviews demonstrated that involving all appropriate stakeholders is crucial for successful RW-PRO implementation. Participants often mentioned that engaging different RW-PRO end users early was essential to success. From its inception, the design of the PRO system should consider the possibility of using collected data to serve multiple purposes.

In my opinion, developing PRO systems that, from their inception, consider multiple applications for collected data is ambitious but worth pursuing. Although creating such a comprehensive system may require significant time and effort, integrating PRO data into the delivery of care and discussing it during medical consultations can mitigate many issues related to maintaining patient participation—issues that are often encountered in PRO initiatives conducted solely for research purposes. Consequently, a complex PRO

system serving multiple purposes should be viewed as the gold standard. Unfortunately, this approach may not always be feasible, and in some cases, a research-oriented PRO data collection might be necessary.

However, using PROs for multiple purposes presents certain challenges. For example, if PRO responses are used to influence healthcare service financing or quality monitoring, there is a potential risk of phenomena similar to upcoding seen in claims databases. Healthcare providers may be incentivised to achieve specific scores, which could impact the validity of PRO results. Some argue that the use of PROs for monitoring care quality, such as pain management, contributed to the opioid crisis in the US. Reusing this type of data for research purposes might undermine its reliability and would necessitate a specific type of data adjustment.

6.3.2.4 Research priorities to advance RW-PRO space

Based on the totality of research conducted as part of the PhD project, it is possible to recommend some research priorities with the potential to substantially contribute to the field. Research priorities which need to be addressed to further advance the RW-PRO space are presented in Table 6.1.

Table 6.1. Research priorities to advance the RW-PRO space.

Nr	Priority
1	To identify existing PRO-specific guidance that is applicable to the RW space. Such recommendations should be extracted and summarised.
2	To identify existing RWE-specific guidance that is applicable to the RW-PRO space. Such recommendations should be extracted and summarised.
3	To explore considerations for determining the validity of PROMs in the RW setting. Characteristics of PROMs, such as recall period or concepts of interest being assessed, might determine the selection of instruments for use within the RW setting. Different features of the RW-PROs might be preferable to those used in traditional RCTs. Future research should guide when additional validation work is required for existing PROMs to be used in the RW setting.
4	To quantify the use of PROs in other types of RWE studies (outside of phase IV clinical trials).
5	To identify strategies aimed to maximise patient engagement, study retention and remote provision of RW-PRO data.
6	To investigate optimal models for financing and operating PRO data collection in routine clinical practice. Multiple stakeholders' perspectives should be considered when proposing operating models for PRO systems.

6.3.3 Inclusive and equitable PRO data collection

RW studies offer promise in enhancing the inclusivity and applicability of health research. By enrolling diverse patient cohorts, RW studies can more accurately reflect the populations targeted by interventions. The collection of real world data presents an opportunity to promote equity and inclusivity in research by extending activities beyond specialised clinical settings to community centres and routine care facilities. However,

designing inclusive data collection methods presents a challenge that requires careful consideration by RW researchers. Fortunately, there is a growing body of evidence focusing on inclusive and equitable data collection practices that should be considered and implemented within the RW setting.[34, 35] Publication 4 delves into more details of the inclusive use of RW-PROs and its benefits for more generalisable healthcare research. It is a comment article formatted and submitted for publication in Nature Reviews Drug Discovery.

6.3.3.1 Publication 4

Konrad Maruszczyk, Olalekan Lee Aiyegbusi, Thomas Keeley, Christel McMullan, Angela J Rylands, Seamus Kent, Onyekachukwu Illoh, Sarah E Hughes, Philip Collis, John Devin Peipert, Melanie J Calvert. The Added Value of Including Patient-Reported Outcomes in Real-World Evidence Research.

Based on the thesis's key findings, the following comment article was submitted for publication in the peer-reviewed journal Nature Reviews Drug Discovery. The manuscript discusses the value of RW-PROs by highlighting their most essential benefits and examining barriers hampering their full implementation. It calls for action to advance the field and briefly presents recommendations for future research.

The Added Value of Including Patient-Reported Outcomes in Real-World Evidence Research

Konrad Maruszczyk[1], Olalekan Lee Aiyegbusi[1-4], Thomas Keeley[1,5], Christel McMullan[1,2], Angela J Rylands[6], Seamus Kent[7], Onyekachukwu Illoh[8], Sarah E Hughes[1-4], Philip Collis[1,9], John Devin Peipert[10], Melanie J Calvert[1-4]

1) Centre for Patient Reported Outcome Research and Birmingham Health Partners Centre for Regulatory Science and Innovation, University of Birmingham, Birmingham, UK
2) NIHR Blood and Transplant Research Unit (BTRU) in Precision Transplant and Cellular Therapeutics, University of Birmingham, Birmingham, UK
3) NIHR Applied Research Collaboration (ARC) West Midlands, University of Birmingham, Birmingham, UK
4) NIHR Birmingham Biomedical Research Centre, University of Birmingham, Birmingham, UK
5) Patient Centered Outcomes, Value Evidence and Outcomes, GlaxoSmithKline (GSK), Brentford, UK
6) Health Economics and Outcomes Research, Kyowa Kirin International, Marlow, UK
7) Erasmus School of Health Policy & Management, Erasmus University Rotterdam, Rotterdam, Netherlands
8) Division of Clinical Outcome Assessment, Office of Drug Evaluation Sciences, Office of New Drugs, Center for Drug Evaluation and Research, Food and Drug Administration, Silver Spring, Maryland, USA
9) Patient partner
10) Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Corresponding author:
Olalekan Lee Aiyegbusi, Assoc. Prof.
E-mail: o.l.aiyegbusi@bham.ac.uk

ORCID IDs:
Konrad Maruszczyk (0000-0002-0173-5020)
Olalekan Lee Aiyegbusi (0000-0001-9122-8251)
Thomas Keeley (0000-0003-1584-9093)
Christel McMullan (0000-0002-0878-1513)
Angela J Rylands (0000-0002-7790-4724)
Seamus Kent (0000-0001-7298-3163)
Onyekachukwu Illoh (0000-0001-9839-2919)
Sarah E Hughes (0000-0001-5656-1198)
John Devin Peipert (0000-0001-5762-7881)
Melanie Calvert (0000-0002-1856-837X)

Standfirst (max. 50 words)

Patient-reported outcomes (PROs) can provide valuable evidence of the long-term benefits, risks, and experience of therapeutics from the patient perspective. Collaborative efforts are required to promote high-quality real-world PRO data collection that is inclusive and equitable to inform regulators, payers, patients, and healthcare professionals.

Introduction

Patient-reported outcomes (PROs) are self-reports of a patient's health, without interpretation of the patient's response by a clinician or anyone else. They can provide valuable information about the experience of living with a disease, the impact of treatment on symptoms, symptomatic treatment side effects, physical function, and health-related quality of life. PRO data from clinical trials are increasingly informing regulatory decision-making and reimbursement.[1]

Randomised Control Trials (RCTs) remain the "gold standard" of clinical investigation. However, the results of RCTs might not be readily generalisable to target patient populations. RCTs test health interventions among selected patient samples within highly controlled conditions. Closely monitored RCTs of pharmaceutical interventions may overestimate real-world treatment benefits due to better patient compliance in a research setting, close follow-up, or a higher standard of concurrent interventions.

The collection of PROs from broader populations, outside the confined setting of clinical trials, allows for real-world evidence (RWE) generation. The publication of RWE-focused frameworks and guidance documents by regulators and payers reiterates the growing interest in utilising RWE to inform market authorisation and reimbursement.[2,3] Although some of these documents highlight the potential benefits of capturing real-world PROs (RW-PROs), they do not provide PRO-specific recommendations.[4]

RWE is useful in the post-approval evaluation of new interventions' long-term effectiveness and safety or to inform label expansion.[5] RWE can also provide valuable input at earlier phases of a product lifecycle, e.g. characterising disease burden, depicting disease progression trajectories, and inputting to the design of subsequent stages of clinical investigation.[6] Increasingly, real-world

studies incorporate PROs along with other types of clinical outcomes to better characterise the benefits and risks of health interventions among target populations. The use of real-world data (RWD) for constructing external control arms for clinical trials when head-to-head comparisons are not feasible is also valuable.

RW-PROs are particularly useful in fields where patients are treated with drugs with a high risk of adverse events. For example, PROs may provide data on the real-world tolerability of cancer treatments. Specifically, PROs can help to describe the safety profile of advanced cell therapies such as CAR-T. Patient perspective is critical for the reporting of side effects of drugs in oncology as these are often underreported and underestimated by clinicians.[12] Also, clinician-reported outcomes and biomarkers might often overlook changes in patient well-being following treatment administration. Other areas might also benefit, especially when some side effects may not be objectively captured, e.g. psychiatry or pain management. Overall, RW-PROs have potential to help us better understand marketed medical products.

RWE to address generalisability

Patients with distinct clinical characteristics, e.g., multiple comorbidities, pregnancy, older age or experiencing rare diseases are often excluded from clinical trials due to stringent inclusion/exclusion criteria. Thus, RWE provides an opportunity to learn about the real-world experience of treatments among patients who better represent the target population.

Moreover, it has been demonstrated that certain patient groups and individuals do not participate in clinical research as readily as others.[7] Different characteristics might induce research exclusion, e.g. ethnicity, social and education status or research distrust, leading to the systematic omission of these patient groups and their underrepresentation in healthcare research. Real-world studies

allow to gather data from these populations. Collecting RWD, possibly as part of routinely provided care, creates an opportunity to include underrepresented sub-groups. Administering PROs in real-world settings should provide more generalisable study results. Nevertheless, collecting RW-PRO data must be inclusive and equitable to deliver that promise.[8]

Inclusive and equitable RW-PRO generation

Although collecting PRO data in a routine care setting creates the opportunity for more equitable research, it should not be assumed that this will be realised. Coordinated efforts are needed to address barriers which hamper inclusive RW-PRO collection. The generalisability of research results may be compromised if data is not collected equitably or inclusively.

Real-world studies need to be designed to represent target populations. Certain considerations need to be given within subject groups to promote inclusive and equitable PRO data collection, including multiple aspects, such as participants' various levels of literacy, cultural and language differences, digital exclusion, and privacy issues.[8]

Different literacy levels should be considered at the stage of PRO instrument development. Questionnaires need to be straightforward and use lay terminology. Moreover, patients should be informed about the purpose of data collection and study benefits to encourage participation. Patients' engagement positively impacts PRO completion rates and data quality. Questionnaires have to obtain crucial information, so study objectives can be met, however the number and length of questionnaires and frequency of administration require careful consideration to reduce respondent burden and data missingness.

Translated and culturally validated PRO questionnaires should be available so they can be understandable by culturally diverse target patient populations. Data collection strategies should

consider the values and preferences of the target population. Awareness of privacy and data protection issues is growing. Researchers should actively consider these factors, as they may be a key decision point for some patients when considering participation.

The mode of data collection should be carefully considered to maximise the quantity and quality of collected PRO data. For example, the level of IT literacy should be factored in. Less computer-literate individuals might prefer to use hard copies of questionnaires or require assistance with electronic data submission. Inequalities in internet access should be considered. Recently, data provided from participants' own devices has been utilised increasingly. Access to such equipment among the target population should be considered. Thus, if possible, multiple modes of data provision should be available to the patients to ensure inclusive PRO data collection. Moreover, accessibility of PRO measures and communication support for responders must be addressed. Assistive technologies such as screen readers, visual or hearing support tools should be used to reach patient groups precluded from self-administration due to disability.

Overall, study design should be tailored to its intended use. Study objectives and perceived value of the PRO data may impact the rigour of data collection. Nevertheless, researchers should strive for equitable and inclusive real-world studies.

Barriers

Realising the benefits of RW-PROs is not straightforward. Multiple barriers exist, both operational and methodological, hampering the full implementation of RW-PROs.[9] Operational challenges are associated with collecting PROs at the individual level and relate to the readiness of infrastructure and organisations to sustain large-scale data collection. Whilst RW-PRO data can be collected through prospective real-world studies, there is also opportunity for sourcing them from electronic

health records in routine care setting. Even if PRO collection as part of routine care is enabled, turning it into research-quality data might be challenging. For example, PRO instruments selected for routine care, and when collected might not always be useful to answer the research question in mind. Also, quality of data collection, influenced in a numerous ways, would be of paramount importance for re-using these data for research.

Methodological barriers are associated with the robustness and interpretability of RW-PRO data, of which there is a dearth of guidance available to support researchers in study design and data analysis.[4] Lack of standards and scarce examples of good practices limit clarity on how these data can be incorporated into decision-making. It reduces the incentives to invest time and money in collecting high-quality RW-PRO data.

Future directions

The scientific community must collectively overcome existing barriers to fully benefit from using RW-PROs for multiple purposes. The field needs to develop and adopt good practices and standards for generating robust RW-PRO data. Dialogue between researchers, clinicians, patient groups, including those from underserved communities, regulators, payers, and the pharmaceutical industry, is vital to achieve this goal. Established standards would be helpful to inform the development of RW-PRO studies. One ongoing initiative that aims to provide multiple-stakeholders consensus-based emerging good practices is the ISPOR Task Force, which focuses on using PROs in prospective real-world study design.

RWE has already demonstrated its value and robustness in supporting label claims on several occasions.[10] It was shown in the label extension regulatory process for tacrolimus to prevent lung transplant rejection.[11] RWE has also been used in regulatory decision-making for drugs targeting

rare diseases: cerliponase alfa for Batten disease, omaveloxolone for the treatment of Friedreich's ataxia and elivaldogene autotemcel for the treatment of adrenoleukodystrophy.[11] To what extent RW-PROs will meet the anticipated prospects in this context remains to be seen.

Conclusion

Real-world studies typically provide information on healthcare resource utilisation, clinical events, and the results of medical examinations. Implementing RW-PROs in this landscape gives a more comprehensive assessment of patients' health status. The importance of patient perspective in evaluating the effects of treatments being scrutinised is paramount.

RW-PROs can offer numerous benefits for healthcare research, such as enhancing understanding of disease and intervention experience from the patient perspective and capturing the tolerability and effectiveness of new products in a broader population. Real-world assessment of new interventions allows for greater generalisability of study findings and careful study design can promote equity and inclusivity in research. To deliver these promises, a joint effort of diverse multidisciplinary stakeholders is needed to overcome barriers hampering the full implementation of PROs for RWE generation.

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9 Maruszczyk, K. *et al.* Paving the way for patient centricity in real-world evidence (RWE): Qualitative interviews to identify considerations for wider implementation of patient-reported outcomes in RWE generation. *Heliyon* **9**, e20157, doi:https://doi.org/10.1016/j.heliyon.2023.e20157 (2023).

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Continued efforts to facilitate inclusive and equitable collection of PRO data are imperative. When designing data collection initiatives, various underserved groups must be considered. Researchers must meticulously assess access to the Internet or electronic devices which are planned to be used for PRO data submission. Moreover, the IT literacy levels of the target population should be considered. Electronic PROMs used should be interoperable with multiple platforms and operating systems.

6.3.4 PRO data collection as part of routine practice

Efforts should also be directed towards tackling operational hurdles that hinder the widespread integration of PRO data collection into routine clinical practice, which remains vastly underutilised. Investments in implementing PRO systems should be proportional to the benefits they bring to involved parties, ensuring adequate resources are allocated to support data collection of this nature. Additional work to develop the optimal infrastructure to facilitate PRO data collection would be advantageous.

Participants of the qualitative study mentioned that the main emphasis should be laid on the readiness of infrastructure to support large-scale data collection. Appropriate resources must be dedicated to harmonising PROs into healthcare providers' workflows. Our findings regarding the possible ways of overcoming operational barriers for PRO uptake are similar to some of the themes described by the previous qualitative work in this area.[36] Some participants mentioned that guidelines and standards facilitating PRO use in routine care are already available.[37-41] These documents should enhance the use of PROs in routine care and indirectly accelerate PRO implementation for RWE generation.

6.4 Strengths and limitations of the thesis

This PhD thesis delves into the exciting and relatively unexplored territory of using PROs to generate RWE. The research offers a valuable contribution to the field, but it's important to consider both its strengths and limitations for a comprehensive understanding.

The mixed methods utilised in this PhD work allow us to answer research questions better and provide an overview of various aspects related to RW-PRO data utilisation. This in-depth exploration equips future researchers with a solid foundation to build upon. The chosen topic has not been attended in such a systematic way before. The significant interest garnered from the research community, culminating in the prestigious JPRO "Article of the Year" award, proves its originality and potential to advance the field. Moreover, this research is significantly contributing to the ongoing ISPOR Task Force work, further demonstrating its novelty and confirming interest in this topic from various stakeholders.

This project's systematic review lays a strong foundation by employing a rigorous methodology for identifying all relevant guidelines and recommendations. The first systematic review in this area establishes a valuable starting point for further research endeavours. The field of RWE is constantly evolving, and new publications are emerging at a rapid pace. Updates to the review will be necessary to capture this ongoing development. Additionally, the potential exclusion of relevant publications due to limitations in database indexing highlights a challenge inherent to such reviews.

The automated search employed in the quantitative analysis of the ClinicalTrials.gov database allows for quick and easy updates in the future, facilitating ongoing monitoring of trends in PRO use. Additionally, using the automated computer algorithm ensures a transparent and replicable method, allowing other researchers to verify and build upon the findings easily. While focusing in this analysis on phase IV trials only poses a simplification, it's essential to acknowledge that RWE encompasses a broader range of study designs. The reliance on the ClinicalTrials.gov database, limited to US-registered trials, potentially overlooks international studies. However, the analysis demonstrates international coverage within the included trials, mitigating this limitation to some extent. Future research might explore incorporating a broader range of study designs and geographically diverse data sources.

In-depth interviews provide rich insights into the motivations and viewpoints of stakeholders, offering a nuanced understanding of their perspectives. Including stakeholders from varied backgrounds enriches the study by capturing multiple viewpoints, from patients to regulators and industry representatives. On the other hand, the recruitment of study participants primarily among enthusiasts of the RWE and PRO fields may introduce bias, affecting the generalisability of findings. Also, restricting patient recruitment to the UK limits the applicability of findings to other geographic regions, potentially limiting the study's relevance on a global scale.

Overall, this PhD thesis's strengths outweigh its limitations. Its comprehensive investigation, innovative methods, and broad dissemination make it a valuable contribution to the field of RWE generation using PROs. By acknowledging the limitations

and suggesting areas for future research, the thesis paves the way for further advancements in this crucial area.

6.5 Conclusions

PROs are less frequently used in RW research compared to earlier clinical investigation phases. PRO can offer several benefits and have the potential to contribute to decision-making processes taking place within healthcare systems. To fully benefit from RW-PROs, various barriers must be overcome during the implementation process. One of the barriers that needs to be addressed is the current lack of standards and guidelines supporting RW-PRO use. Collaborative efforts are needed to advance the field and allow for inclusive PRO data collection and its use in decision-making.

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Appendices

Appendix 2.1: Patient experts' consent form

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CONSENT FORM (Patient interviews)

Study Title: Best Practice For Implementation Of PROs In Real World Evidence Generation: Qualitative study

Thank you for agreeing to take part in this study, please ensure that you have read the information sheet that you have been given (RWE_PRO_participant_information_sheet_PAT.pdf) and asked any and all questions you might have. If you are satisfied with the information you have received, please read each sentence below and **initial** the box next to the sentence if you agree. Finally please sign and date the bottom of the form:

Participant number _____ *Participant initials* _____

Item of consent	*Please initial each box*
The study has been explained to me, and I have read and understood the participant information sheet (RWE_PRO_participant_information_sheet_PAT.pdf) any questions I had about the study and interview process have been answered.	
I have been informed that it is my right to refuse to take part in the study today, and that if I choose to refuse I do not have to give a reason. Also, if I wish to withdraw my data, I can do so up to 5 working days after the interview has taken place.	
I have been informed that anything I say during the interview today will remain completely confidential: my name will not be used, neither will any other information that could be used to identify me.	
It has been explained that the researchers will use my own words when writing up the findings of this research. I understand that any use of my words would be completely anonymous.	
I agree that anonymised copies of interview transcripts will be held securely at The University of Birmingham and may be used for future related research.	
I am willing to be contacted for future related research, and my participation in these will be voluntary.	

I consent voluntarily to be a participant in this study:

Signature of participant:

NAME (in capital letters)	SIGNATURE	DATE OF SIGNATURE (in DD/MM/YYYY)

Signature of interviewer:

NAME (in capital letters)	SIGNATURE	DATE OF SIGNATURE (in DD/MM/YYYY)

Appendix 2.2: Other experts' consent form

UNIVERSITY OF BIRMINGHAM | COLLEGE OF MEDICAL AND DENTAL SCIENCES

CPROR

CONSENT FORM (Stakeholder interviews)

Study Title: Best Practice For Implementation Of PROs In Real World Evidence Generation: Qualitative study

Thank you for agreeing to take part in this study, please ensure that you have read the information sheet that you have been given (STA_information_sheet.docx) and asked any and all questions you might have. If you are satisfied with the information you have received, please read each sentence below and **initial** the box next to the sentence if you agree. Finally please sign and date the bottom of the form:

Participant number _____ *Participant initials* _____

Item of consent	*Please initial each box*
The study has been explained to me, and I have read and understood the participant information sheet (STA_information_sheet.docx) any questions I had about the study and interview process have been answered.	
I have been informed that it is my right to refuse to take part in the study today, and that if I choose to refuse I do not have to give a reason. Also, if I wish to withdraw my data, I can do so up to 5 working days after the interview has taken place.	
I have been informed that anything I say during the interview today will remain completely confidential: my name will not be used, neither will any other information that could be used to identify me or my organisation.	
It has been explained that the researchers will use my own words when writing up the findings of this research. I understand that any use of my words would be completely anonymous.	
I agree that anonymised copies of interview transcripts will be held securely at The University of Birmingham and may be used for future related research.	
I am willing to be contacted for future related research, and my participation in these will be voluntary.	

I consent voluntarily to be a participant in this study:

Signature of participant:

NAME (in capital letters)	**SIGNATURE**	**DATE OF SIGNATURE** (in DD/MM/YYYY)

Signature of interviewer:

NAME (in capital letters)	**SIGNATURE**	**DATE OF SIGNATURE** (in DD/MM/YYYY)

Appendix 2.3: Patient experts' participant information sheet

Best Practice For Implementation Of PROs In Real World Evidence Generation: Qualitative study

Introduction

Professor Melanie Calvert, Dr Olalekan Lee Aiyegbusi and PhD student Konrad Maruszczyk alongside other colleagues from the Centre for Patient-Reported Outcomes at the University of Birmingham would like to invite you to participate in this study.

In research, we increasingly use questionnaires to assess participant's symptoms and quality of life. These types of information are known as patient-reported outcomes (PROs). They represent health status reported directly by the patient, without interpretation by a clinician or anyone else. However, we also need to understand how medical treatments affect many more people outside clinical trials which often involves a limited number of people. We call this real-world evidence generation (RWE). We would like to understand your views about collecting this longer-term information on patient symptoms and quality of life in routine medical practice to assess if a treatment is working and if it is safe for the patients.

Our overall aim is to better understand the use of patient-reported data in the long-term studies of drugs following the completion of clinical trials. Patients' perspectives will be crucial to describe different aspects associated with the collection and utilisation of PRO data.

Why is this study being done?

The information generated within long-term studies of drugs following the completion of clinical trials is increasingly often used to support drug registration or reimbursement processes. This kind of data allows us to assess if a treatment works and if it is safe for

diverse patient populations. Information collected directly from patients about their symptoms and quality of life should be used to enrich these datasets. To maximise the benefits associated with the use of this kind of data, a better understanding of different aspects of its collection and use is needed.

As part of this project, patient interviews and focus groups give us a chance to capture your opinion on the use of PRO data in the long-term studies of drugs after the completion of clinical trials. Moreover, it helps to better understand patients' needs and hopes associated with the wider collection and use of PRO data.

Who is eligible to take part?

Patients over 18 years old who can provide consent. You are not obliged to take part and should you chose to participate you can withdraw from the study at any time without any consequence to the care you are receiving.

What will happen if I take part in this study?

We would like to ask you some questions about your perspectives on issues associated with PROs utilisation in the long-term studies of drugs after the completion of clinical trials. We expect the interview or focus group to last a maximum of 60 minutes, however, there is no time limit if you do have more to say. We will take notes of the discussion and an audio recording will also be made using both an online conference platform built-in recording feature and a digital voice recorder. All information gathered will be treated as confidential by the interviewers, and records of the interviews will be kept securely in locked filing cabinets and offices. No personal identification information such as names will be used in any reports arising out of this study. The information you provide will not be fed back to physicians managing your care.

What are the potential benefits of taking part?

Your participation will allow for a deeper understanding of how PROs are currently used in routine clinical practice. It will also help us to identify the barriers and facilitators of PRO collection from a patient perspective. Additionally, you will be reimbursed for travel costs (if applicable) and your time at the rate of £20 per hour (in form of vouchers).

What are the potential risks of taking part?

Participation involves a remote conversation via a platform for online meetings. It will not present any physical risks to you though the information may be discussed which might be considered sensitive. However, the confidentiality of the discussion will be ensured. No data will be presented which identifies a specific organisation, or participant instead each individual involved will be given a code by the interviewer. These codes will be used when presenting the results of the study for publication, and any quotes used in the publication will have any identifying information, such as names, removed.

Will my participation be confidential and information secure?

University of Birmingham is the sponsor for this study based in the United Kingdom. We will be using information gathered from you during the interview or focus group to undertake this work and we will act as the data controller. This means that we are responsible for looking after your information and using it properly.

All information gathered will be completely confidential. No names will be recorded and instead, each participant and their organization will be given a code and this will be used to present the information. Only the interviewer will be able to link the code to a specific participant. All data collected will be kept securely, with hard copies in locked and secure facilities and digital data stored and encrypted on secure data storage devices.

University of Birmingham will keep identifiable information about you from this study for 10 years after it has finished. This data will be only accessible to the interviewers and the research team; data will be stored for 10 years before being destroyed. No other sites will retain personal or study data.

All information gathered will be treated as confidential by the interviewers, and records of the interviews will be kept securely in locked filing cabinets and offices. No personal identification information such as names will be used in any reports arising out of this study. The information you provide will not be fed back to any other organisation. You can find out more about how we use your information by contacting University of Birmingham's Information Compliance Manager on legalservices@contacts.bham.ac.uk

Can I withdraw from the study?

You can decide to stop participating at any time. Just tell the interviewer right away if you wish to stop. You do not need to give a reason for your withdrawal. Nevertheless, if you participate in a focus group discussion it will be impossible to withdraw your data during or after the discussions because participants will be audio recorded as a group. However, you are free to stop contributing and leave. If you participate in a one-to-one interview and ask for the interview to be stopped, the interviewer will ask if you are happy for the data given up to that point to be used. If you would like all the data to be deleted, just tell the researcher. For the interview - you are also able to withdraw your data up to 5 working days after the interview. To do so please contact Konrad Maruszczyk by email (ktm095@student.bham.ac.uk).

What if there is a problem?

If you have any complaints about your treatment as a participant during the course of the study or any harm you feel has been caused to you, this can be addressed by either contacting the interviewer directly to discuss these concerns or if this is not appropriate then you are asked to follow the university complaints procedure, by contacting the University of Birmingham Research Ethics Officer. Furthermore, this study is being undertaken with the support of the University of Birmingham and as such the university has provided insurance to cover compensation that this study may incur.

Who has reviewed this study?

The study has been reviewed and approved by the University of Birmingham's Science, Technology, Engineering and Mathematics (STEM) ethics committee. All such projects are approved by the STEM committee to ensure that due process has been described and will be met. If you have any questions or issues that you would like to raise you are encouraged to discuss them with an interviewer, either via telephone or video call or the e-mail addresses provided.

Centre for Patient Reported Outcome Research (CPROR)

Institute of Applied Health Research

Room 219, The Murray Learning Centre

Primary Care & Clinical Sciences

University of Birmingham

Edgbaston

Birmingham B15 2TT

United Kingdom

Telephone: +44 (0)121 414 3354
Fax: +44 (0)121 414 3353

Prof. Melanie Calvert

By Telephone: 0121 414 8595

By Email: m.calvert@bham.ac.uk

Dr Olalekan Lee Aiyegbusi

By Telephone: 0121 415 8324

By Email: O.L.Aiyegbusi@bham.ac.uk

Konrad Maruszczyk

By Email: ktm095@student.bham.ac.uk

University of Birmingham Ethics Team

Sam Waldron, Deputy Research Ethics Officer

By Email: s.m.waldron@bham.ac.uk

Appendix 2.4: Other experts' participant information sheet

Best Practice For Implementation Of PROs In Real World Evidence Generation: Qualitative study

Introduction

Professor Melanie Calvert, Dr Olalekan Lee Aiyegbusi and PhD student Konrad Maruszczyk alongside other colleagues from the Centre for Patient-Reported Outcomes at the University of Birmingham are conducting an exploration of how real-world evidence (RWE) generation can be enhanced by the collection and use of Patient-Reported Outcomes (PROs). Efforts are being made to better understand how different aspects related to PRO data collection, analysis and use should be approached to maximise the potential benefits of implementing PROs for RWE generation.

Why is this study being done?

RWE plays an increasingly important role within global regulatory and reimbursement processes. RWE studies are used to assess the real-world long-term effectiveness and safety of health interventions in diverse patient populations. Unlike the highly controlled environment of registration trials, which are usually limited to specialised health care providers, characterised by artificially high patient compliance and close patient monitoring.

By definition, PROs represent health status as reported directly by the patient, without interpretation by a clinician or anyone else. PROs are usually collected via questionnaires that elicit information about symptoms, physical functioning and/or health-related quality of life.

RWE generation can be enhanced by the collection and use of PROs. PROs can provide valuable information on the effectiveness, safety and tolerability of health interventions from the patient perspective. However, currently, the collection of PRO data in the real-world setting is restricted. Researchers have limited guidance to support the use of PROs in RWE generation. Available recommendations are fragmented and

there is a lack of international guidelines for the collection and utilisation of PROs in this context.

As part of this project, key stakeholders (including health care professionals (HCPs), health care providers, regulators, payers and manufacturers) interviews and focus groups will be conducted to learn about their previous experiences with using PROs and the barriers and facilitators of utilising PRO data for RWE generation.

Who is eligible to take part?

Health care professionals (HCPs), health care providers, regulators, payers and manufacturers with a keen interest in PRO use in real world setting. You are not obliged to take part and should you chose to participate you can withdraw from the study at any time.

What will happen if I take part in this study?

We would like to ask you some questions about your perspective on issues around collection and use o PRO data for RWE generation. We expect the interview or focus group to last a maximum of 60 minutes, however there is no time limit if you do have more to say. We will take notes of the discussion and an audio recording will also be made using both an online conference platform built-in recording feature and a digital voice recorder. All information gathered will be treated as confidential by the interviewers, and records of the interviews and focus groups will be kept securely in locked filing cabinets and offices. No personal identification information such as names or affiliations will be used in any reports arising out of this study. The information you provide will not be fed back to your organisations.

What are the potential benefits of taking part?

Your participation will allow for a deeper understanding of how PROs are currently used in routine clinical practice. It will also help us to identify the barriers and facilitators of PRO collection based on your previous experiences.

What are the potential risks of taking part?

Participation involves a remote conversation via a platform for online meetings. It will not present any physical risks to you though it is possible that information may be discussed which might be considered sensitive. However, the confidentiality of the discussion will be ensured. No data will be presented which identifies a specific organisation, or participant instead each individual involved will be given a code by the interviewer. These codes will be used when presenting the results of the study for publication, and any quotes used in the publication will have any identifying information, such as names, removed.

Will my participation be confidential and information secure?

University of Birmingham is the sponsor for this study based in the United Kingdom. We will be using information gathered from you during the interview or focus group to undertake this work and we will act as the data controller. This means that we are responsible for looking after your information and using it properly.

All information gathered will be completely confidential. No names will be recorded and instead, each participant and their organization will be given a code and this will be used to present the information. Only the interviewer will be able to link the code to a specific participant. All data collected will be kept securely, with hard copies in locked and secure facilities and digital data stored and encrypted on secure data storage devices.

University of Birmingham will keep identifiable information about you from this study for 10 years after it has finished. This data will be only accessible to the researcher and the

research team; data will be stored for 10 years before being destroyed. No other sites will retain personal or study data.

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Can I withdraw from the study?

You can decide to stop participating at any time. Just tell the interviewer right away if you wish to stop. You do not need to give a reason for your withdrawal. Nevertheless, if you participate in a focus group discussion it will be impossible to withdraw your data during or after the discussions because participants will be audio recorded as a group. If you participate in a one-to-one interview and ask for the interview to be stopped, the interviewer will ask if you are happy for the data given up to that point to be used. If you would like all the data to be deleted, just tell the researcher. For the interview - you are able to withdraw your data up to 5 working days after the interview. To do so please contact Konrad Maruszczyk by email (ktm095@student.bham.ac.uk).

What if there is a problem?

If you have any complaints about your treatment as a participant during the study or any harm you feel has been caused to you, this can be addressed by either contacting the interviewer directly to discuss these concerns or if this is not appropriate then you are asked to follow the university complaints procedure, by contacting the University of Birmingham Research Ethics Officer. Furthermore, this study is being undertaken with the support of the University of Birmingham and as such the university has provided insurance to cover compensation that this study may incur.

Who has reviewed this study?

The study has been reviewed and approved by the University of Birmingham's Science, Technology, Engineering and Mathematics (STEM) ethics committee. All such projects are approved by the STEM committee to ensure that due process has been described and will be met. If you have any questions or issues that you would like to raise you are encouraged to discuss them with the interviewer, either via telephone or video call or the e-mail addresses provided.

Centre for Patient Reported Outcome Research (CPROR)

Institute of Applied Health Research

Room 219, The Murray Learning Centre

Primary Care & Clinical Sciences

University of Birmingham

Edgbaston

Birmingham B15 2TT

United Kingdom

Telephone: +44 (0)121 414 3354
Fax: +44 (0)121 414 3353

Prof. Melanie Calvert

By Telephone: 0121 414 8595

By Email: m.calvert@bham.ac.uk

Dr Olalekan Lee Aiyegbusi

By Telephone: 0121 415 8324

By Email: O.L.Aiyegbusi@bham.ac.uk

Konrad Maruszczyk

By Email: ktm095@student.bham.ac.uk

University of Birmingham Ethics Team

Sam Waldron, Deputy Research Ethics Officer

By Email: s.m.waldron@bham.ac.uk

Appendix 2.5: Matrixes with record of framework matching

CFIR

			Participation and engagement			Stakeholder collaboration					Data collection and management						
	Domains/Themes	Instrument selection	Study participation	Study development and conduct	Burden to HCPs and patients	Study design	Setting an international approach to PRO assessment	Patient-centred care	Education and training	PRO implementation process	Frequency of data collection	Integration with other databases	Data audit	Data ownership	Electronic data capture	Impact of disease progression on data collection	Data analysis and presentation of results
Intervention Characteristics	Intervention Source			x		x				x							
	Evidence Strength and Quality	x						x									
	Relative Advantage	x							x								
	Adaptability			x	x	x				x	x	x			x	x	
	Trialability			x		x				x							
	Complexity	x	x		x	x				x	x	x					
	Design Quality and Packaging	x		x		x				x		x	x		x		
	Cost									x							
Outer Setting	Patient Needs and Resources		x	x	x			x	x							x	
	Cosmopolitanism						x										
	Peer Pressure					x			x								x
	External Policies and Incentives						x	x		x		x					x
Inner Setting	Structural Characteristics				x					x					x		
	Networks and Communications								x	x							
	Culture				x				x	x							
	Implementation Climate				x				x	x							
	Tension for Change							x									
	Compatibility	x						x		x							
	Relative Priority					x		x		x							
	Organizational Incentives and Rewards				x				x	x							
	Goals and Feedback									x							
	Learning Climate								x	x							
	Readiness for Implementation									x							
	Leadership Engagement								x	x							
	Available Resources				x				x								
	Access to Knowledge and Information								x	x							
Characteristics of Individuals	Knowledge and Beliefs about the Intervention	x	x			x											
	Self-efficacy		x		x	x					x						
	Individual Stage of Change		x		x					x							
	Individual Identification with Organization				x												
	Other Personal Attributes				x				x								
Process	Planning									x							
	Engaging								x								x
	Opinion Leaders								x	x							
	Formally Appointed Internal Implementation Leaders								x	x							
	Champions								x	x							
	External Change Agents								x	x							
	Key Stakeholders																
	Innovation Participants																
	Executing									x							
	Reflecting and Evaluating								x	x							x

TFA

		Participation and engagement			Stakeholder collaboration					Data collection and management						
Domains/Themes	Instrument selection	Study participation	Study development and conduct	Burden to HCPs and patients	Study design	Setting an international approach to PRO assessment	Patient-centred care	Education and training	PRO implementation process	Frequency of data collection	Integration with other databases	Data audit	Data ownership	Electronic data capture	Impact of disease progression on data collection	Data analysis and presentation of results
Affective attitude	x	x	x		x											
Burden				x												
Perceived effectiveness	x	x	x		x				x							
Ethicality		x	x		x				x							
Intervention coherence	x		x		x				x							
Opportunity cost		x		x												
Self-efficacy		x		x										x		

RE-AIM

		Participation and engagement			Stakeholder collaboration					Data collection and management						
Domains/Themes	Instrument selection	Study participation	Study development and conduct	Burden to HCPs and patients	Study design	Setting an international approach to PRO assessment	Patient-centred care	Education and training	PRO implementation process	Frequency of data collection	Integration with other databases	Data audit	Data ownership	Electronic data capture	Impact of disease progression on data collection	Data analysis and presentation of results
Reach		x					x									
Efficacy							x									
Adoption		x		x					x							
Implementation		x							x							
Maintanance							x	x	x							

Appendix 3.1: PRISMA 2020 checklist

Additional file 1. PRISMA 2020 Checklist

Section and Topic	Item #	Checklist item	Location where item is reported
TITLE			
Title	1	Identify the report as a systematic review.	Title page
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Title page
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Introduction
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Introduction, paragraph 5-6
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Methods, Search strategy and study selection section
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Methods, Search strategy and study selection section
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	S1 Protocol

Section and Topic	Item #	Checklist item	Location where item is reported
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Methods, Search strategy and study selection section
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Methods, Data extraction section
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Methods, Data extraction section
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Methods, Data extraction section
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Methods, Data extraction section
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Methods, Data extraction section
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Results, Recommendations issued section
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Results, Recommendations issued section
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	Results, Recommendations issued section
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	N/A
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Figure 1
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Methods, Scope of the review
Study characteristics	17	Cite each included study and present its characteristics.	Table 2
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	N/A
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	N/A
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Results, Recommendations issued section
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	N/A
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	N/A
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	Discussion, Conclusion
	23b	Discuss any limitations of the evidence included in the review.	Limitations
	23c	Discuss any limitations of the review processes used.	Limitations
	23d	Discuss implications of the results for practice, policy, and future research.	Discussion
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Abstract; Methods, paragraph
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	S1 Protocol
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A

Section and Topic	Item #	Checklist item	Location where item is reported
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	Funding information
Competing interests	26	Declare any competing interests of review authors.	Competing interests
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	S1 Protocol, S2 Table

Appendix 3.2: Search strategy

Additional file 2. Search strategy

Inclusion/exclusion criteria

Criteria	Inclusion	Exclusion
Research area	Real-world data/evidence/research	Clinical setting
Outcome	• PRO	Other types of outcomes
Study type	• Guidelines • Recommendations	Other types of studies
Date	No limit	None
Countries	All	None
Publication type	Full research reports in journals, reports, discussion papers and books, commentaries, editorials	Letters, notes, news (publication type)
Language	English language studies[a]	Non-English language studies

[a] English abstracts of non-English language studies will be considered for inclusion

Search strategy

Medline search terms (Searched on 18/01/2021)

#	Criteria	Search term	Hits
1	Research area	real-world.ab,kf,kw,ti.	30509
2		RWE.ab,kf,kw,ti.	172
3		exp Pragmatic Clinical Trials as Topic/	560

4		OR 1-3	31012
5		exp Health Status Indicators/	313292
6		exp Health Status/	350958
7		exp "Quality of Life"/	202456
8		exp "Severity of Illness Index"/	258115
9		exp Self-Assessment/	12664
10		(self-report$ or self report$).ab,kf,kw,ti.	136939
11		functional.ab,kf,kw,ti.	1068421
12		patient reported.ab,kf,kw,ti.	27488
13		OR 5-12	1771468
14	Outcome	outcome$.ab,kf,kw,ti.	1512012
15		experience$.ab,kf,kw,ti.	947903
16		measure$.ab,kf,kw,ti.	2852540
17		assess$.ab,kf,kw,ti.	2621781
18		(score$ or scoring).ab,kf,kw,ti.	841557
19		index.ab,kf,kw,ti.	674277
20		indices.ab,kf,kw,ti.	136671
21		scale$.ab,kf,kw,ti.	668812
22		monitor$.ab,kf,kw,ti.	703154
23		OR 14-22	7243628

24		13 AND 23	886956
25		exp Patient Reported Outcome Measures/	7234
26		(qol or 'health-related quality of life' or 'hrqol' or 'quality of life' or 'nasal symptoms' or rhinitis or wpai or 'work loss' or 'opportunity loss' or productivity or depression or anxiety or 'global impression' or sleep or insomnia or 'burden of illness' or 'impact of disease' or 'patient based outcome' or 'patient experience' or 'patient perception' or 'patient relevant outcome' or 'patient-reported outcome' or 'patient reported outcome*' or 'pro' or 'attitude' or 'patient satisfaction' or 'preference' or 'satisfaction' or 'treatment attitude' or 'treatment importance' or 'treatment priorit*' or 'treatment perception').ab,kf,kw,ti.	1205425
27		OR 24-26	1854966
28	Study type	exp Consensus/	14149
29		exp Consensus Development Conference/	12171
30		exp Guideline/	34166
31		exp Practice Guideline/	27159
32		exp Health Planning Guidelines/	4120
33		exp Practice Guideline as Topic/	121541
34		(guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.	43688
35		(position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kf,kw.	28140
36		(standards or guideline or guidelines).ti,kf,kw.	97563
37		((practice or treatment* or clinical) adj guideline*).ab.	34714
38		(CPG or CPGs).ti.	5337

39		consensus*.ti,kf,kw.	22750
40		recommendat*.ti,kf,kw.	37235
41		OR 28-40	299125
42	N/A	4 AND 27 AND 41	**246**

Embase search terms (Searched on 18/01/2021)

#	Criteria	Search term	Hits
1	Research area	real-world.ab,kw,ti.	79881
2		RWE.ab,kw,ti.	830
3		exp pragmatic trial/	1034
4		OR 1-3	80996
5	Outcome	exp Health Status Indicator/	32453
6		exp Health Status/	249609
7		exp "Quality of Life"/	516418
8		exp "Severity of Illness Index"/	18180
9		exp self evaluation/	32895
10		(self-report$ or self report$).ab,kw,ti.	216858
11		functional.ab,kw,ti.	1604037
12		patient reported.ab,kw,ti.	67216
13		OR 5-12	2498755

14		outcome$.ab,kw,ti.	2731006
15		experience$.ab,kw,ti.	1560392
16		measure$.ab,kw,ti.	4409929
17		assess$.ab,kw,ti.	4441189
18		(score$ or scoring).ab,kw,ti.	1602984
19		index.ab,kw,ti.	1183191
20		indices.ab,kw,ti.	204115
21		scale$.ab,kw,ti.	1158398
22		monitor$.ab,kw,ti.	1161844
23		OR 14-22	11704957
24		13 AND 23	1319671
25		exp patient-reported outcome/	27724
26		(qol or 'health-related quality of life' or 'hrqol' or 'quality of life' or 'nasal symptoms' or rhinitis or wpai or 'work loss' or 'opportunity loss' or productivity or depression or anxiety or 'global impression' or sleep or insomnia or 'burden of illness' or 'impact of disease' or 'patient based outcome' or 'patient experience' or 'patient perception' or 'patient relevant outcome' or 'patient-reported outcome' or 'patient reported outcome*' or 'pro' or 'attitude' or 'patient satisfaction' or 'preference' or 'satisfaction' or 'treatment attitude' or 'treatment importance' or 'treatment priorit*' or 'treatment perception').ab,kw,ti.	2057687
27		OR 24-26	2909937
28	Study type	exp Consensus/	75713

29		exp Consensus Development/	24880
30		exp Practice Guideline/	579489
31		'Health Planning Guideline'.ti,ab,kw.	2
32		(guideline or practice guideline or consensus development conference or consensus development conference, NIH).ti,ab,kw.	100407
33		(position statement* or policy statement* or practice parameter* or best practice*).ti,ab,kw.	51923
34		(standards or guideline or guidelines).ti,ab,kw.	159319
35		((practice or treatment* or clinical) adj guideline*).ab.	64569
36		(CPG or CPGs).ti.	7082
37		consensus*.ti,kw.	35153
38		recommendat*.ti,kw.	55504
39		OR 28-38	858890
40	N/A	4 AND 27 AND 39	**1207**

Appendix 3.3: Data extraction

Additional file 3. Data extraction

PRO Guidelines - Data extraction form

Author	Year	Instrument selection	Standard sets	Participation and engagement	Burden to health care professionals and patients	Stakeholder collaboration	Education and training	PRO implementation process	Data collection and management	Data analysis and presentations of results
Hanson et al.	2020	Pragmatic trial investigators can promote the development of new brief PCROs (Patient Carer Reported Outcomes), or pragmatic adaptation of existing PCROs. Exemplary standard set of clinical outcome measures suitable for people living with dementia (PLWD) were proposed. Existing brief PCROs may need adaptation or language translation to ensure acceptability in culturally diverse populations. Investigators who use existing PCROs will need to create shortened versions to make data collection feasible and reliable.	Yes	Outcome measures should: address patient or caregiver-centered outcome domain; be acceptable to patients or their care partners; have demonstrated importance to other key stakeholders, such as health system leadership; meet psychometric standards for validity, reliability, and responsiveness/sensitivity to change; and demonstrate pragmatic properties, such as feasibility and low respondent burden.	Design features of many instruments used to capture PCROs impede pragmatic use. Written questionnaires or interviews typically impose high respondent burden, and are rarely tested in real-world clinical settings for wide-scale application. Examples include computer adaptive testing to reduce the item burden for self-report by PLWD, smart phone applications that facilitate PCRO reporting, use of automated interactive voice response telephone calls to collect data from PLWD who do not have internet access, and wearable devices that capture data on activity or function.	Outcome measures should have demonstrated importance to other key stakeholders such as health system leadership. An investigator may require stakeholder engagement to design a novel pragmatic PCRO.	Creation of libraries of clinical outcomes suitable for PLWD was postulated.		Some clinical electronic health records (EHRs) now provide a platform into which brief PCROs can be embedded, and many have system-wide embedded PCROs, such as depression screening tools. In addition, EHRs permit clinicians or practice groups to customize clinical encounter templates, and these pathways have the potential to facilitate real-world clinical data capture of brief or pragmatic PCROs. Methods used to embed PCROs for data capture in large data sets, such as the MDS, may be replicated for data capture of carefully selected PCROs in EHRs or clinical registries. Emerging practices for novel data capture may facilitate Alzheimer's Disease (AD)/Alzheimer's Disease Related Dementias(ADRD) ePCTs (embedded pragmatic clinical trials). Examples include computer adaptive testing to reduce the item burden for self-report by PLWD, smart phone applications that facilitate PCRO reporting, use of automated interactive voice response telephone calls to collect data from PLWD who do not have internet access, and wearable devices that capture data on activity	
Calvert et al.	2019	The questionnaire(s) used to collect the data should be relevant and valid for the objectives, the population of interest and meet stakeholder needs. Questionnaires should have been developed with patient input. Consider inclusion of patients from diverse backgrounds.	No	Language availability, patient acceptability/burden, permissions and fee for use should also be considered.	Minimize workload and technical complexity for patients, clinicians and health providers.	Ensure international collaboration across multiple stakeholders including patients, caregivers, clinicians, regulators, ethicists, industry, payers and policy makers to agree to a standardized approach to PRO assessment.		Determine who pays for license fees, training, data collection, clinic time, device costs etc.	Frequency will depend on stakeholder needs and the study population. Patients with high symptom burden may require more frequent monitoring. The data collection plan should outline the permitted modes of administration (for example, paper, telephone, electronic, other). Utilise electronic capture wherever appropriate. It should be considered whether PRO data will be monitored and used to directly inform patient care. Consider primary or secondary collection. Feasibility and resources to support data collection, existing registries, electronic health records, requirement for bespoke collection. Specify management strategies to minimise missing data and bias. Methods to ensure quality control. IT infrastructure may be based on existing system or customised / commercial products. Mechanisms for on-going audit of data quality etc. should be considered.	The data should be analysed and reported appropriately, in accordance with the prospective described objectives and the instrument recommendations, leading to robust conclusions considering potential sources of bias/confounding. Provide guidance on how to interpret and use the data.
Rylands et al.	2018	Patients literacy skills should be assessed whe	No	The level of contact patients have with healthcare services will impact recruitment methodologies and may affect levels of patient engagement with the study. Optimal frequency and timing of PRO data collection should be proposed.	Minimisation of patient burden: the frequency of patient-reported outcome (PRO) measurement and subsequent follow-up must be limited to the necessary minimum in RW studies so as not to impact routine clinical care.				RW studies cannot influence the scheduling of clinic visits which is likely to impact the timing and method of PRO measurement. Study design: the choice of a retrospective or prospective design, and potentially the amount of missing data, will be influenced by whether PRO data are routinely collected in clinical practice. Whether and how PROs are currently being used in clinical practice determines the likelihood of obtaining robust PRO data. Patients ability to self-report should be assessed when designing RW study. Reliability of proxy reporting should be determined. Toolkit for study design and conduction was proposed.	

Kyte et al.	2016	Ensure the evidence base for patient-reported outcome measure (PROMs) selected for use in the clinical setting is definitive and includes patient input.	No			PROM data collected were hoped to influence patients decision on health care provider selection.	Guidance on how best to interpret and utilise the data should be given.	The taskforce believed greater patient benefit/cost-effectiveness could be derived by shifting focus from the current 'top-down' national PROMs initiative, to a more efficient 'bottom-up' clinic-based collection of PROMs data that could be used for multiple purposes. Such data could be utilised at a macro level, not only to monitor outcomes, but also to inform big data research, prognostic modelling, post-marketing surveillance and development of patient decision aids. Utilise electronic capture wherever appropriate.	Ensure there is clarity on how the data will be used. This needs to be made explicit in communications with patients.	Give providers guidance on how best to interpret and utilise the data. Methodologically rigorous process should be in place to determine optimal way of results dissemination.
The Association of the British Pharmaceutical Industry (ABPI)	2011		No			Involve all relevant stakeholders and expertise. Designing RW projects commonly require input from a variety of stakeholders both within Pharma and external. Internally this may include, although not limited to, a multidiscipline approach with Medical Affairs, Clinical Development, health economics, brand teams, pharmacovigilance, statistical and regulatory departments. External expert input during the design process may be valuable in assessing feasibility of the design, data evidence collection and data statistical considerations.		The use of PROs in RW studies might cause that, it will meet the definition of interventional clinical trials of medicinal products. Thus it will need to comply with The Medicines & Healthcare products Regulatory Agency (MHRA) applies the 'Medicines for Human Use (clinical trials) Regulations 2004', (amended 2006) (which is derived from the EU Clinical Trials Directive(EUCTD) 2001). If true, Clinical Trials Authorisation (CTA) needs to be obtained from MHRA. Where patient reported outcome measure (PROM) questionnaires, or clinician rating scales that are not in routine use in normal clinical practice, are to be used to obtain data in study, careful consideration should be given as to whether their use would constitute an 'additional diagnostic or monitoring procedure' within the terms of the Directive and if necessary advice can be obtained from the MHRA.	Clarification of who owns the rights to any data or any potential intellectual property generated. Clarification of how long data should be stored and by whom and under what conditions. Data collected via RW projects are often kept for shorter time periods than clinical trials.	Consideration should be given as to how the statistical analysis is performed. This may include generation of a database, data cleaning activities and statistical methods.
Akiyama et al.	2015	Pilot test with elderly patients to assess feasibility and comprehension to make sure the elderly precisely understand and fill in the questionnaires properly should be conducted.	No	Additional support required at the participating sites for elderly patients. Large letters, simple wording should be used for explanatory document and questionnaire. Strategise recruitment of physicians depending on their environment and resources available: general practitioners vs. hospital physicians Recruitment of HCPs with interest in PROs. Institution capacity and resources needed to conduct research need to assisted before recruitment. Reinforce cross-functional collaboration in order to accelerate site recruitment, patient enrolment and the return of patient surveys. Posters and flyers should be used to promote the study and encourage health care professionals (HCPs) to participate.		Deepen the understanding of the value of PRO assessments and contents of PRO questionnaires among internal/external stakeholders. Internal collaboration and close communication with study sites are critical.	Prior and continuous training through different channels, materials and tools are necessary. Lack of understanding of the value of PRO assessments for marketed products among internal and/or external stakeholders, despite increasing use of PRO tools in regulatory studies. Maintenance of motivation and understanding of the study procedures in relevant healthcare professionals throughout the study period is crucial. Advise from clinical experts should be obtained and integrated into training materials.	Process map describing four stages: internal discussion, design and preparation, implementation and dissemination was proposed.	Reminders sent from the Electronic Data Capture (EDC) system and reminders through Medical Representatives can be used to accelerate collection of patient surveys and data entry in case report form (CRF). Reconsider the use of e-PRO even for the elderly. Large letters, simple wording should be used for explanatory document and questionnaire. Since elderly patients are more likely to have declined cognitive function, HCPs are concerned that it is difficult to find patients who can answer self-administered questionnaires.	
Banerjee et al.	2013		Yes (a core minimum dataset for non-regulated consumer sites was proposed)		Internet and digital media should be screened for patient reports on suspected adverse reactions. Priority should be given to the more serious safety issues. The use of smartphone apps for reporting is already underway in developing countries and allows greater freedom in data capture. When deciding about data collection through smart technologies (e.g. phones, smartphones, tablets) following areas should be considered: 1. Access to technology; 2. Data privacy and storage issues; 3. Appropriateness for the population; 4. Data transmission; 5. Cost; 6. Technical awareness of patients—since the dataset will be biased if only technically aware patients report; 7. Patient knowledge of the ability to report and patient willingness to report; 8. Data privacy and protection.			Need to accept non-medically confirmed adverse events (AEs) reported directly by patients.	Suitable study data set need to be established, regulated consumer sites or some patient support sites allow for structured data collection. Patient centric dictionary needs to be considered for PRO-AE data collection. PRO-AE-enabled websites allow a more structured approach providing higher quality of data. Safety variables should be collected as comprehensively as possible including type of AE, severity, onset and duration. PRO-AE-enabled websites allow a more structured approach providing higher quality of data. Suitable study data set need to be established, regulated consumer sites or some patient support sites allow for structured data collection. Data protection legal requirements need to be met.	Information collected from non-prespecified populations and non-structured datasets need to be balanced against quantitative validity. PRO-AE data can be analysed independently or in combination with AE information form other sources. Additional safety evaluations may be needed in specific subpopulations, such as females, the elderly, the severely ill, or those who have a common concomitant treatment. Statistical methods suitable for post-approval, non-prespecified datasets were proposed.

Appendix 4.1: Removed search terms

Appendix 1. Removed search terms

Lp.	PROMs	Composite measures
1	can	vs
2	care	vss
3	cost	fast
4	first	
5	mrs	
6	probe	
7	brief	
8	case	
9	able	
10	air	
11	speed	
12	mood	
13	direct	
14	pasi	
15	soc	
16	pfs	
17	flare	
18	exact	
19	aim	
20	ease	
21	map	
22	psa	
23	aims	
24	mini	
25	bis	
26	cis	
27	hands	
28	das	
29	tof	
30	she	
31	sas	
32	fas	
33	quick	

Appendix 4.2: PROMs search term list

Appendix 2. PROMs search term list

id	names
0	SCOPA-PS
0	Scales for Outcomes in Parkinson's Disease - Psychosocial functioning
1	PQLQ-PM
1	Patient Quality Of Life Questionnaire (Physical & Emotional) - Peritoneal Malignancies
2	MASRI
2	Medication Adherence Self-Report Inventory
3	PSSD
3	Psoriasis Signs and Symptoms Diary
4	MPS-HAQ
4	MPS Health Assessment Questionnaire
5	RPQ
5	Rivermead Post-Concussion Symptoms Questionnaire
6	MG-QoL15
6	Myasthenia Gravis Quality of Life 15-item Scale
7	Liq.In7 record
7	Liquid Intake 7-Day Record
8	CVAQC
8	Cardiff Visual Ability questionnaire for Children
9	VAQ
9	Visual Activities Questionnaire
10	LLQ
10	Low Luminance Questionnaire
11	SCS
11	Symptom Catastrophizing Scale
12	CushingQoL
12	Cushing's disease quality of life instrument
13	ABS-A

13	Atopic dermatitis burden scale for Adults
14	MSKCC BFI
14	Memorial Sloan Kettering Cancer Centre Bowel Function Instrument
15	TBI-QOL SF
15	Traumatic Brain Injury – Quality of Life Short form
16	SCI-QOL SF
16	Spinal Cord Injury – Quality of Life Short form
17	Pediatric Neuro-QOL
17	Pediatric version of the Quality of Life in Neurological Disorders
18	CTCL-QoL
18	Mycosis Fungoides/Sezary Syndrome - Cutaneous T-cell lymphoma Quality of life
19	SWN-S
19	Subjective Well-being under Neuroleptic treatment - Short Form
20	SCOPA-AUT
20	Scales for Outcomes in Parkinson’s Disease - Autonomic dysfunction
21	PDQ-Carer
21	Parkinson's Disease Questionnaire for Carer
22	FTND-ST
22	Fagerström Test for Nicotine Dependence for Smokeless Tobacco Users
23	KDQ
23	Kidney Disease Questionnaire
24	Neuro-QOL
24	Quality of Life in Neurological Disorders
25	SWLS
25	Satisfaction With Life Scale
26	PCOSQ
26	Polycystic Ovary Syndrome Questionnaire
27	SOAPP
27	Screener and Opioid Assessment for Patients with Pain
28	FACIT-D
28	Functional Assessment of Chronic Illness Therapy for Patients With Diarrhea

29	Pediatric Neuro-QOL SF
29	Pediatric version of the Quality of Life in Neurological Disorders Short Form
30	IIQ
30	Incontinence Impact Questionnaire
31	GOS
31	Global Overall Symptom scale
32	PQLQ-S
32	Patient Quality Of Life Questionnaire (Physical & Emotional) - Sarcoma
33	PAH-SYMPACT
33	Pulmonary Arterial Hypertension-Symptoms and Impact (PAH-SYMPACT) Questionnaire
34	WPAI:CD
34	Work Productivity and Activity Impairment Questionnaire in Crohn's Disease
35	PDDS
35	Patient Determined Disease Steps
36	PBPI
36	Pain Beliefs and Perceptions Inventory
37	FBI
37	Family Burden Ichthyosis questionnaire
38	HDISS-DU
38	Hand Disability In Systemic Sclerosis - Digital Ulcers
39	NFCSI-19
39	National Comprehensive Cancer Network Functional Assessment of Cancer Therapy Colorectal Symptom Index- 19 items
40	ODS Score
40	Obstructed Defaecation Syndrome Score
41	PinQ
41	Pediatric Incontinence Questionnaire
42	S-HTS
42	Sheehan-Homicidality Tracking Scale
43	S-PGI
43	Sheehan-Patient Global Improvement Scale
44	SCOPA-PC

44	Scales for Outcomes in Parkinson’s Disease - Psychiatric disturbances
45	FPS-R
45	Faces Pain Scale - Revised version
46	MPAI-4
46	Mayo-Portland Adaptability Inventory
47	GALES
47	The Geriatric Adverse Life Events Scale
48	MG-ADL
48	Myasthenia Gravis Activities of Daily Living Profile
49	ZKPQ III-R
49	Zuckerman-Kuhlman Personality Questionnaire III-Revised
50	RLIES
50	Revised Liverpool Impact of Epilepsy Scale
51	Haemo-SYM
51	Haemo-SYM
52	BPI-SF
52	Brief Pain Inventory - Short form
53	PSI-SF
53	Parenting Stress Index - Short Form
54	Wexner Scale
54	Wexner Cleveland Clinic Incontinence Score
55	SPS
55	Sheehan-Panic Disorder Scale
56	URAM Scale
56	Unité Rhumatologique des Affections de la Main Scale
57	PR-SMFIS
57	Patient-Reported Submental Fat Impact Scale
58	OABSS
58	Overactive Bladder Symptom Score
59	FACT-C
59	Functional Assessment of Cancer Therapy-Colorectal cancer

60	PDQ-D
60	Perceived Deficits Questionnaire – Depression
61	PROMIS Short Form v1.0 - Fatigue 7b Daily
61	Patient-Reported Outcomes Measurement Information System Short Form v1.0 - Fatigue 7b Daily
62	DRS-PI
62	Disability Rating Sale – Postacute Interview
63	TBI-QOL
63	Traumatic Brain Injury – Quality of Life
64	HD-PRO-TRIAD
64	HD-PRO-TRIAD
65	Haemo-QoL-A
65	Hemophila-specific Quality of Life Questionnaire for Adults
66	SOAPP-R
66	Screener and Opioid Assessment for Patients with Pain - Revised version
67	QLiS
67	Quality of Life in Schizophrenia
68	FQOL
68	Beach Center Family Quality of Life Scale
69	PSST/PSST-A
69	Premenstrual Symptoms Screening Tool
70	HDQLIFE
70	Huntington's Disease health-related Quality of LIFE
71	ICIQ-MLUTS
71	ICIQ-Male Lower Urinary Tract Symptoms (Short form)
72	OxPAQ
72	Oxford Participation and Activities Questionnaire
73	PROMIS SexFS Bank v2.0 – Vaginal Discomfort
73	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v2.0 – Vaginal Discomfort
74	PROMIS SexFS Bank v2.0 – Lubrication
74	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v2.0 – Lubrication

75	PROMIS SexFS Bank v2.0 – Orgasm
75	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v2.0 – Orgasm
76	PROMIS SexFS Pool v2.0 - Therapeutic Aids
76	PROMIS Sexual Function and Satisfaction Pool v2.0 - Therapeutic Aids
77	Ped-CDSD
77	Pediatric-Celiac Disease Daily Symptom Diary
78	WPAI:Neuropathic Pain
78	Work Productivity and Activity Impairment Questionnaire:Neuropathic Pain
79	WPAI:NASH
79	Work Productivity and Activity Impairment Questionnaire: NonAlcoholic SteatoHepatitis or Fatty Liver, V2.0
80	FACIT-Dyspnea
80	Functional Assessment of Chronic Illness Therapy - Dyspnea
81	FPI
81	Functional Performance Inventory
82	TSI-2
82	Trauma Symptom Inventory-2
83	TSCC-SF
83	Trauma Symptom Checklist for Children - Screening Form
84	16D
84	16-dimensional health-related quality of life measure
85	SIS-16
85	Stroke Impact Scale
86	LEC-5
86	Life Events Checklist for DSM-5
87	SIQ
87	Suicidal Ideation Questionnaire
88	DAPS
88	Detailed Assessment of Posttraumatic Stress
89	EGQ-D
89	Esophago-Gastric surgery and Quality of Dietary life

90	PROMIS SexFS Bank v2.0 – Erectile Function
90	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v2.0 – Erectile Function
91	PROMIS SexFS Bank v2.0 – Global Satisfaction with Sex Life
91	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v2.0 – Global Satisfaction with Sex Life
92	PROMIS SexFS Bank v2.0 – Interest in Sexual Activity
92	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v2.0 – Interest in Sexual Activity
93	PROMIS SexFS Pool v2.0 - Anal Discomfort
93	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v2.0 - Anal Discomfort
94	PROMIS SexFS Profile v2.0 – Male & Female
94	PROMIS Sexual Function and Satisfaction Profile v2.0 – Male & Female
95	FAQ
95	Gillette Functional Assessment Questionnaire
96	17D
96	17-dimensional health-related quality of life measure
97	WPAI:Menopause
97	Work Productivity and Activity Impairment Questionnaire: Menopausal Symptoms, Version 2
98	SIS v3.0
98	Stroke Impact Scale
99	ASIQ
99	Adult Suicidal Ideation Questionnaire
100	ES4
100	Esophagus and Stomach Surgery Symptom Scale
101	PROMIS SexFS Pool v2.0 - Interfering Factors
101	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v2.0 - Interfering Factors
102	PROMIS SexFS Pool v2.0 - Sexual Activities
102	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v2.0 - Sexual Activities
103	PROMIS SexFS Pool v2.0 - Sexual Function Screener
103	PROMIS Sexual Function and Satisfaction Pool v2.0 - Sexual Function Screener

104	BWSQ
104	Benzodiazepine Withdrawal Symptom Questionnaire
105	OCDUS-C
105	Obsessive Compulsive Drug Use Scale cocaine version
106	DDQ-C
106	Desire for Drug Questionnaire cocaine version
107	TSCC
107	Trauma Symptom Checklist for Children
108	HypoA-Q
108	Hypoglycaemia Awareness Questionnaire
109	RCAT
109	Rhinitis Control Assessment Test
110	WPAI:LBP
110	Work Productivity and Activity Impairment Questionnaire:Lower Back Pain
111	WPAI:UC
111	Work Productivity and Activity Impairment Questionnaire:Ulcerative Colitis
112	WPAI:CD-CG
112	Work Productivity and Activity Impairment Questionnaire: Crohn's Disease, for caregivers, Version 2.0
113	DRRI-2
113	Deployment Risk & Resilience Inventory-2
114	GIS
114	Global Improvement Scale
115	ICIQ-LUTSqol
115	ICIQ-Lower Urinary Tract Symptoms Quality of Life
116	UDI
116	Urogenital Distress Inventory
117	EORTC QLQ-CR38
117	EORTC Quality of Life Questionnaire - Colorectal Cancer Module
118	ASCQ-Me SF
118	Adult Sickle Cell Quality of Life Measurement Information System Short Form
119	SOWS-Gossop

119	Short Opiate Withdrawal Scale-Gossop
120	ICDSQ
120	Impact of Celiac Disease Symptoms Questionnaire
121	PGH-7 Parent-Proxy Form
121	PROMIS - Pediatric Global Health Parent-Proxy Form
122	CLEFT-Q
122	CLEFT-Questionnaire
123	PROMIS Pediatric Profile-49 v2.0
123	Patient-Reported Outcomes Measurement Information System Pediatric Profile-49 v2.0
124	PROMIS Pediatric Profile-37 v2.0
124	Patient-Reported Outcomes Measurement Information System Pediatric Profile-37 v2.0
125	IBSQoL
125	Irritable Bowel Syndrome Quality of Life Questionnaire
126	MAQ-PC
126	Multimorbidity Assessment Questionnaire for Primary Care
127	DPQ
127	Dallas Pain Questionnaire
128	MRI-AQ
128	Magnetic Resonance Imaging-Anxiety Questionnaire
129	JCS
129	Jackson Cold Scale
130	FANLTC
130	Functional Assessment of Non-Life Threatening Conditions
131	FHNSI
131	Functional Assessment of Cancer Therapy-Head and Neck Symptom Index
132	WPAI:IBS
132	Work Productivity and Activity Impairment: Irritable Bowel Syndrome
133	WPAI:AS
133	Work Productivity and Activity Impairment: Allergy Specific
134	WPAI:RA
134	Work Productivity and Activity Impairment - Rheumatoid Arthritis

135	MDASI-MM
135	MD Anderson Symptom Inventory - Multiple Myeloma Module
136	Behavior Rating Inventory of Executive Function
137	CHRT-SR7
137	Concise Health Risk Tracking Self-Report scale - 7 item self-report
138	ICIQ- FLUTSsex
138	ICIQ-Female Sexual Matters associated with Lower Urinary Tract Symptoms
139	CDSD 2.1
139	Celiac Disease Symptom Diary
140	PROMIS SexFS v2.0 Full Profile (Female)
140	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction v2.0 Full Profile (Female)
141	PROMIS SexFS v2.0 Brief Profile (Female)
141	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction v2.0 Brief Profile (Female)
142	QUALMS
142	Quality of Life in Myelodysplasia Scale
143	FACT-Br
143	Functional Assessment Of Cancer Therapy - Brain
144	FAPSI
144	Functional Assessment of Cancer Therapy - Advanced Prostate Symptom Index - 8 Item version
145	MDASI-HN
145	MD Anderson Symptom Inventory - Head and Neck Cancer Module
146	BRIEF-SR
146	Behavior Rating Inventory of Executive Function - Self-Report Version
147	CCBS-2
147	Child's Challenging Behaviour Scale, Version 2
148	Cdiff32
148	Clostridium difficile Questionnaire
149	RTES
149	Recent Traumatic Events Scale
150	CIVIQ-14

150	Chronic Lower Limb Venous Insufficiency Questionnaire - 14 items
151	ICIQ-MLUTSsex
151	ICIQ-Male Sexual Matters associated with Lower Urinary Tract Symptoms
152	PROMIS PF10
152	PROMIS Physical Function 10
153	DVSS
153	Dysfunctional Voiding Scoring System
154	SAPS for PDP
154	Scale for Assessment of Positive Symptoms for Parkinson's disease psychosis
155	PROMIS Pediatric Profile-25 v2.0
155	Patient-Reported Outcomes Measurement Information System Pediatric Profile-25 v2.0
156	FACIT-Fatigue
156	Functional Assessment of Chronic Illness Therapy - Fatigue Scale
157	PROMIS SexFS v2.0 Brief Profile (Male)
157	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction v2.0 Brief Profile (Male)
158	PPMQ-R
158	Patient Perception of Migraine Questionnaire-Revised
159	FACT-MM
159	Functional Assessment of Cancer Therapy - Multiple Myeloma
160	FBSI
160	Functional Assessment of Cancer Therapy-Breast Symptom Index
161	WPAI:CHRI
161	Work Productivity and Activity Impairment: Child's Hospitalization for Respiratory Illness
162	MDASI-BT
162	MD Anderson Symptom Inventory - Brain Tumor Module
163	MDASI-GIST
163	MD Anderson Symptom Inventory - Gastrointestinal Stromal Tumor Module
164	MDASI-HF
164	MD Anderson Symptom Inventory - Heart Failure Module
165	MDASI-SP
165	MD Anderson Symptom Inventory - Spine Tumor Module

166	MDASI-TCM
166	MD Anderson Symptom Inventory - Traditional Chinese Medicine Module
167	OSD-QoL
167	Ocular Surface Disease - impact of OSD on HRQoL
168	ICIQ-MLUTS LF
168	ICIQ-Male Lower Urinary Tract Symptoms (Long form)
169	SQLS R4
169	Schizophrenia Quality of Life Scale Revision 4
170	PROMIS-57 Profile v2.1
170	Patient-Reported Outcomes Measurement Information System - 57 Profile v2.1
171	HDQ
171	HIV Disability Questionnaire
172	LFQ
172	Lung Function Questionnaire
173	BIRS
173	Body Image and Relationships Scale
174	Patient's Self-Assessment Grading Scale
175	FACT-HN
175	Functional Assessment of Cancer Therapy - Head & Neck cancer
176	FHSI
176	Functional Assessment of Cancer Therapy - Hepatobiliary Symptom Index
177	WPAI:GERD
177	Work Productivity and Activity Impairment: Gastro-Esophageal Reflux Disease
178	MDASI-Thy
178	MD Anderson Symptom Inventory - Thyroid Cancer Module
179	ASEC
179	Antidepressant Side-Effect Checklist
180	ABNAS
180	A–B Neuropsychological Assessment Schedule
181	ASCQ-Me
181	Adult Sickle Cell Quality of Life Measurement Information System

182	ISI-P
182	Incontinence Symptom Index-Pediatric
183	NHQ
183	Noctural Hypokinesia Questionnaire
184	GIQLI-10
184	Gastrointestinal Quality of Life index - 10 items
185	PROMIS-43 Profile v2.1
185	Patient-Reported Outcomes Measurement Information System - 43 Profile v2.1
186	ASK-12
186	Adherence Starts with Knowledge 12
187	AML-QOL
187	Quality of Life in Acute Myeloid Leukemia
188	MEI-SF
188	Motivation and Energy Inventory-Short Form
189	FACT-NP
189	Functional Assessment of Cancer Therapy - Nasopharyngeal cancer
190	MICRA
190	Multidimensional Impact of Cancer Risk Assessment
191	WPAI:SpA
191	Work Productivity and Activity Impairment - Ankylosing Spondylitis
192	WALS
192	Workplace Activity Limitations Scale
193	MDASI-GI
193	MD Anderson Symptom Inventory - Gastrointestinal Cancer Module
194	CTQ
194	Childhood Trauma Questionnaire
195	BRIEF2
195	Behavior Rating Inventory of Executive Function, Second Edition
196	CTES
196	Childhood Traumatic Events Scale
197	5-D Pruritus Scale

197	5-D Itch Scale
198	MDASI-AML
198	M.D. Anderson Symptom Inventory - Acute Myeloid Leukemia
198	MDASI-MDS
198	M.D. Anderson Symptom Inventory - Myelodysplastic Syndromes
199	IGFDQ
199	Impact of a Gluten-Free Diet Questionnaire
200	MPFID
200	Migraine Physical Function Impact Diary
201	CHEQOL
201	Health Related Quality of Life in Children with Epilepsy - Child self-report scale
202	GenPs-SFQ
202	Genital Psoriasis Sexual Frequency Questionnaire
203	GPSS
203	Genital Psoriasis Symptoms Scale
204	PROMIS-29 Profile v2.1
204	Patient-Reported Outcomes Measurement Information System - 29 Profile v2.1
205	ASK-20
205	Adherence Starts with Knowledge 20
206	CU-Q2oL
206	Chronic Urticaria Quality of Life questionnaire
207	PAM-D
207	Perceptions About Medications for Diabetes
208	CSS-21
208	21-item Challenges to Stopping Smoking
209	NIH Toolbox - Emotion Battery
209	NIH Toolbox - Emotion Battery
210	MDASI-CML
210	MD Anderson Symptom Inventory - Chronic Myeloid Leukemia Module
211	MDASI-LC
211	MD Anderson Symptom Inventory - Lung Cancer Module

212	BRIEF-A
212	Behavior Rating Inventory of Executive Function - Adult Version
213	RASQ
213	Rituximab Administration Satisfaction Questionnaire
214	CHU9D
214	Child Health Utility
215	QPCQ
215	Quality of Prenatal Care Questionnaire
216	RAPID3
216	Routine Assessment of Patient Index Data 3
217	PROMIS SexFS v2.0 Full Profile (Male)
217	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction v2.0 Full Profile (Male)
218	SNS
218	Self-evaluation of Negative Symptom
219	RPC-Scale
219	Rating of Perceived Capacity
220	FACT-G7
220	Functional Assessment of Cancer Therapy - General (7-item version)
221	FACT-GP
221	Functional Assessment of Cancer Therapy - General Population
222	FACT-V
222	Functional Assessment of Cancer Therapy - Vulva cancer
223	Quality of Life in Children with Vernal Keratoconjunctivitis
224	WPAI:ChHD
224	Work Productivity and Activity Impairment - Chronic Hand Dermatitis
225	MDASI-CGVHD
225	MD Anderson Symptom Inventory - Chronic Graft-Versus-Host Disease module
226	MDASI-OC
226	MD Anderson Symptom Inventory - Ovarian Cancer Module
227	NutriQoL
227	NutriQoL

228	PPQ
228	Patient Preference Questionnaire
229	CADSS
229	Clinician-Administered Dissociative States Scale
230	CIVIQ-20
230	Chronic Lower Limb Venous Insufficiency Questionnaire - 20 items
231	BISF-W
231	Brief Index of Sexual Functioning for Women
232	AMA
232	About My Asthma
233	AQLQ-NAA
233	Asthma Quality of Life Questionnaire for Native American Adults
234	MUDI
234	Male Urogenital Distress Inventory
235	FFI
235	Foot Function Index
236	ONYCHO
236	Onychomycosis Quality of Life questionnaire
237	DAN-PSS-1
237	Danish Prostatic Symptom Score
238	MILQ
238	Multidimensional Index of Life Quality
239	SFS2
239	Social Functioning Scale
240	APMG-15
240	Attitudes Professionnelles des Médecins Généralistes
241	TLFB
241	Timeline Followback Method
242	CRFDS
242	Cancer-Related Fatigue Distress Scale
243	N-QoL

243	Nocturia Quality of Life Questionnaire
244	EPIC
244	Expanded Prostate Cancer Index Composite
245	Menopause Rating Scale
246	CBS
246	Cardiff Breast Scales
247	MRQ
247	Menopause Representations Questionnaire
248	MUSIQ
248	Male Urinary Symptom Impact Questionnaire
249	SCS
249	Smoker Complaint Scale
250	VHI
250	Voice Handicap Index
251	NEI-RQL-42
251	National Eye Institute - Refractive Error Quality of Life Instrument - 42
252	W-QLI
252	Wisconsin Quality of Life Index
253	MOS-HIV
253	Medical Outcome Study-HIV Health Survey
254	HLQ
254	Health and Labour Questionnaire
255	QOL-AD
255	Quality of Life in Alzheimer’s Disease
256	YQOL
256	Youth Quality of Life Instrument
257	PAS
257	Panic and Agoraphobia Scale
258	WPAI:GH 2.0
258	Work Productivity and Activity Impairment Questionnaire: General Health V2.0
259	AVFT

259	Arabic Visual Function Test
260	NEI-VFQ-25
260	National Eye Institute Visual Function Questionnaire-25
261	MFI
261	Multidimensional Fatigue Inventory
262	JSEQ
262	Jenkins Sleep Evaluation Questionnaire
263	MM-CGI
263	Marwit Meuser Caregiver Grief Inventory
264	LSEQ
264	Leeds Sleep Evaluation Questionnaire
265	FLIE
265	Functional Living Index - Emesis
266	CHILD-OIDP or C-OIDP
266	Child-Oral Impact on Daily Performance Index
267	QLI
267	Ferrans and Powers Quality of Life Index
268	QL-Index
268	Spitzer's Quality of Life Index
269	JAQQ
269	Juvenile Arthritis Quality of Life Questionnaire
270	HANA
270	Headache Needs Assessment questionnaire
271	Harvard Department of Psychiatry/NDSD scale
272	DIAD
272	Diagnostic Interview for Atypical Depression
273	UQOL
273	Utian Quality of Life scale
274	CLAU-S
274	Claudication Scale
275	UIHI

275	Urinary Incontinence Handicap Inventory
276	IWQOL-Lite
276	Impact of Weight on Quality of Life - Lite
277	QOLIE-AD-48
277	Quality of Life in Epilepsy Inventory-Adolescents-48
278	MMQL - Youth Form
278	Minneapolis-Manchester Quality of Life instrument - Youth Form
279	IDEEL
279	Impact of Dry Eye on Everyday Life
280	QOLAS
280	Quality of Life Assessment Schedule
281	AQEL
281	Assessment of Quality of life at the End of Life
282	UFS-QOL
282	Uterine Fibroid Symptom and Quality of Life questionnaire
283	FKB-20
283	BIQ-20
283	Fragebogen zum Körperbild/Body Image Questionnaire
284	Care-Notebook
284	Care Notebook
285	ESRD-SCL-TM
285	End-Stage Renal Disease Symptom Checklist- Transplantation Module
286	OAB-q
286	OverActive Bladder questionnaire
287	LSIA
287	Life Satisfaction Index for Adolescents
288	MOQ
288	Menorrhagia Outcomes Questionnaire
289	Fall Risk Index
289	Fall Risk Index
290	QOLIE-31

290	Quality of Life in Epilepsy Inventory-31
291	GSFQ
291	GERD Symptom Frequency Questionnaire
292	SFSS
292	Structural-Functional Social Support Scale
293	DQOLY
293	Diabetes Quality of Life for Youth scale
294	XQ
294	Xerostomia-specific Questionnaire
295	TOPS
295	Treatment Outcomes in Pain Survey
296	SAT-16
296	SAT-16
297	HIV-SI or SDM
297	HIV Symptom Index
298	mRS-SI
298	Structured Interview for the Modified Rankin Scale
299	CCVUQ
299	Charing Cross Venous Ulcer Questionnaire
300	MDI
300	Major Depression Inventory
301	ESS
301	Epworth Sleepiness Scale
302	Conners 3-SR
302	Conners 3 Self Report Full Length
303	DQOL
303	Diabetes Quality of Life measure
304	QUEST
304	Quality of End-of-life care and Satisfaction with Treatment scale
305	OIDP
305	Oral Impact on Daily Performance Index - modified version

306	GO-QOL
306	Graves' Ophtalmopathy Quality of Life Questionnaire
307	ICIQ-UI Short Form
307	International Consultation on Incontinence Questionnaire - Urinary Incontinence Short Form
308	MIDAS-35
308	Myocardial Infarction Dimensional Assessment Scale
309	WURSS
309	Wisconsin Upper Respiratory Symptom Survey
310	NEWQOL
310	Quality of Life in Newly Diagnosed Epilepsy measure
311	MTAP
311	Multidimensional Task Ability Profile
312	MCAS
312	Modified Caregiver Appraisal Scale
313	QOLIE-10
313	Quality of Life in Epilepsy Inventory-10
314	CHIP
314	Child Health and Illness Profile
315	FOSQ
315	Functional Outcomes of Sleep Questionnaire
316	Conners CBRS Self-Report Form
316	Conners Comprehensive Behavior Rating Scales Self-Report Form
317	WOSI
317	Western Ontario Shoulder Instability Index
318	CCQ
318	Clinical COPD Questionnaire
319	NEWSQOL
319	Newcastle Stroke-specific Quality of Life measure
320	MENQOL
320	Menopause-specific Quality of Life Questionnaire
321	QOL-RTI

321	Quality of Life Radiation Therapy Instrument
322	SSI and SII
322	Symptom Severity Index and Symptom Impact Index for stress incontinence in women
323	YIPS
323	York Incontinence Perceptions Scale
324	WHO-5
324	WHO (Five) Well-Being Index
325	MSQLI
325	Multiple Sclerosis Quality of Life Inventory
326	MQ
326	Menorrhagia Questionnaire
327	ICIQ-FLUTS
327	International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms
328	CSFQ
328	Changes in Sexual Functioning Questionnaire
329	MGQ
329	Myasthenia Gravis Questionnaire
330	KIDSCREEN
330	KIDSCREEN
331	STAR-SMOQ55
331	Situation X Trait Adaptative Response Smoking Motivation questionnaire
332	CARES
332	Cancer Rehabilitation Evaluation System
333	CMSH-SFQ
333	Center for Marital and Sexual Health Sexual Functioning Questionnaire
334	CSQ
334	Client Satisfaction Questionnaire
335	DCSQ
335	Diabetes Clinic Satisfaction Questionnaire
336	DHI
336	Dizziness Handicap Inventory

337	DIS-IV
337	Diagnostic Interview Schedule - IV
338	CAQs
338	Childhood Asthma Questionnaires
339	BUPP
339	Burke Perceptual Profile
340	CHP
340	Cardiac Health Profile
341	COMTol
341	Comparison of Ophthalmic Medications for Tolerability Questionnaire
342	COOP-C or COOP/WONCA
342	COOP/WONCA Charts
343	DAS-3
343	Diabetes Attitude Scale (third version)
344	DKT
344	Diabetes Knowledge Test
345	BPHII
345	Benign Prostatic Hyperplasia Impact Index
346	BPQ
346	Breathing Problems Questionnaire
347	CASC
347	Comprehensive Assessment of Satisfaction with Care
348	CHAL
348	Quality of Life Questionnaire for Arterial hypertension
349	ITSQ
349	Insulin Treatment Satisfaction Questionnaire
350	COVD
350	College of Optometrists in Vision Development Quality of Life Outcomes Assessment
351	PRWE
351	Patient-Rated Wrist Evaluation
352	DFS

352	Diabetic Foot Ulcer Scale
353	DQoLS
353	Dermatology Quality of Life Scales
354	MBI
354	Modified Barthel Index
355	CAS
355	Constipation Assessment Scale
356	CFQ
356	Cystic Fibrosis Questionnaire
357	DEFS
357	Dutch Exertion Fatigue Scale
358	D-FISQ
358	Diabetes Fear of Injecting and Self-testing Questionnaire
359	DHP-1
359	Diabetes Health Profile
360	DKQ
360	Diabetes Knowledge Questionnaire
361	DLQI
361	Dermatology Life Quality Index
362	BFI
362	Brief Fatigue Inventory
363	CHQ
363	Child Health Questionnaire
364	CMV-EYE
364	Quality of Life with Eye Disease
365	CQOLC
365	Caregiver Quality of Life Index-Cancer
366	CPNS
366	Cancer Patient Need Survey
367	DSMP
367	DSMP-F

367	Diabetes Self-Management Profile
368	BHI
368	Brief Hospice Inventory
369	Comprehensive Assessment and Referral Evaluation
370	DASI
370	Duke Activity Status Index
371	DES
371	Diabetes Empowerment Scale
372	DQLCTQ
372	Diabetes Quality of Life Clinical Trial Questionnaire
373	BASIS-32
373	Behavior and Symptom Identification Scale
374	BCTSQ
374	Brigham and Women's Hospital Carpal Tunnel Syndrome Questionnaire or Boston Carpal Tunnel Syndrome Questionnaire
375	GDS
375	Geriatric Depression Scale
376	CRQ
376	Chronic Respiratory Disease Questionnaire
377	DCP
377	Diabetes Care Profile
378	BSI
378	Brief Symptom Inventory
379	CDC HRQOL-14
379	Centers for Disease Control and Prevention Health-Related Quality of Life Measure
380	CDLQI
380	Children's Dermatology Life Quality Index
381	CES-D
381	Center for Epidemiologic Studies Depression Scale
382	COPE
382	COPE
383	DSC-R

383	Diabetes Symptom Checklist-Revised
384	DSFI
384	Derogatis Sexual Functioning Inventory
385	BCQ
385	Breast Cancer Chemotherapy Questionnaire
386	BPD
386	Brief Pain Diary for ambulatory patients with advanced cancer
387	BPI
387	Brief Pain Inventory
388	CDS
388	Cardiac Depression Scale
389	CHQ
389	CHFQ
389	Chronic Heart Failure Questionnaire
390	Contilife
390	Quality of Life Assessment Questionnaire Concerning Urinary Incontinence
391	DFBS
391	Diabetes Family Behavior Scale
392	DIMS
392	Diabetes Impact Measurement Scales
393	DISF
393	Derogatis Interview for Sexual Functioning
394	D-QoL
394	Dementia Quality of Life Instrument
395	DSQL-Acne
395	Dermatology-Specific Quality of Life Instrument for Acne
396	DSQOLS
396	Diabetes specific quality of life scale
397	PROFAD-SSI
397	Profile of Fatigue and Discomfort-Sicca Symptoms Inventory
398	QoL.BD & Brief-QOL.BD

398	Quality of Life in Bipolar Disorder
399	PROFAD-SSI-SF
399	Profile of Fatigue and Discomfort - Sicca Symptoms Inventory - Short Form
400	iMCQ
400	iMedical Consumption Questionnaire
401	PCS-P
401	Pain Catastrophizing Scale - Parent version
402	PCS-S
402	Pain Catastrophizing Scale - Significant Other
403	PGA or SGA
403	Patient's or Subjective Global Assessment Scale
404	LDIQ
404	Lupus Damage Index Questionnaire
405	FLI
405	Functional Living Index - adapted to type 2 diabetes
406	MQOL
406	McGill Quality of Life Questionnaire
407	mHAQ
407	The Modified Health Assessment Questionnaire
408	RBQOLS
408	Rectal Bleeding Quality Of Life Scale
409	QOLI
409	Quality of Life Interview
410	T-IEQ
410	Trait Injustice Experience Questionnaire
411	COMI
411	Core Outcome Measures Index
412	DASH
412	Disabilities of Arm, Shoulder and Hand Questionnaire
413	QuickDASH
413	Quick version of the Disabilities of Arm, Shoulder and Hand Questionnaire

414	BSDI
414	Blepharospasm Disability Index
415	DS-II
415	Demoralization Scale-II
416	CHQ
416	Cluster Headache Quality of Life Scale
417	BCS
417	Body Concept Scale
418	HOOS-PS
418	Hip Disability and Osteoarthritis Outcome Score-Physical Function Short form
419	L-QoL
419	Systemic Lupus Erythematosus Quality of Life
420	PEmb-QoL
420	Pulmonary Embolism Quality of Life Questionnaire
421	PDQ
421	Psychosexual Daily Questionnaire
422	CTS-6
422	6-item Carpal Tunnel Symptoms Scale
423	ASES
423	American Shoulder and Elbow Surgeons Standardized Shoulder Assessment Form
424	FACT-O
424	Functional Assessment of Cancer Therapy - Ovarian Cancer
425	NFOSI-18
425	National Comprehensive Cancer Network Functional Assessment of Cancer Therapy - Ovarian Symptom Index
426	CAARS
426	Conners' Adult ADHD Rating Scale
427	PGI-C, PGI-I, PGI-S
427	Patient Global Impressions scale - Change, Improvement, Severity
428	FACT-CNS
428	Functional Assessment of Cancer Therapy - Central Nervous System
429	Block Fat Screener

429	Block Dietary Fat Screener
430	FMI-8
430	Freiburg Mindfulness Inventory-8
431	EORTC QLQ-PAN26
431	EORTC Quality of life Questionnaire - Pancreatic Cancer Module
432	HDQLIFE Scale v2.0 - Meaning and Purpose
432	HDQLIFE Scale v2.0 - Meaning and Purpose
433	TASQ
433	Toronto Aortic Stenosis Quality of Life Questionnaire
434	TIC-P
434	Treatment Inventory of Costs in Patients with psychiatric disorders
435	RDC/TMD
435	Research Diagnostic Criteria for TemporoMandibular Disorders
436	PHQ-2
436	Patient Health Questionnaire-2 items
437	C-19ASS
437	COVID-19 Anxiety Syndrome Scale
438	VERITAS-Pro
438	Validated Hemophilia Regimen Treatment Adherence Scale-Prophylaxis
439	WSAS
439	Work and Social Adjustment Scale
440	B-IVI
440	Brief Impact of Vision Impairment
441	A-IQOLS
441	Asthma Impact on Quality of Life Scale
442	PCSI
442	Prostate Cancer Peer Support Inventory
443	PCSS
443	Prostate Cancer Symptom Scale
444	SCS
444	Self-Control Scale

445	FDQ
445	Functional Disability Questionnaire
446	OMDQ-25
446	Oromandibular Dystonia Questionnaire
447	HADLI
447	Headache Activities of Daily Living Index
448	PF-IQOLS
448	Pulmonary Fibrosis Impact on Quality of Life Scale
449	PFDI-20
449	Pelvic Floor Distress Inventory-20
450	U-FIS
450	Unidimensional Fatigue Impact Scale
451	MATHYS
451	Multidimensional Assessment of Thymic States
452	PR-PCSS
452	Patient Reported Photonumeric Cellulite Severity Scale
453	Block FV Screener
453	Block Dietary Fruit/Vegetable Screener
454	EORTC QLQ-HL27
454	EORTC Quality of Life Questionnaire - Hodgkin Lymphoma Module
455	Bluebelle WHQ
455	Bluebelle Wound Healing Questionnaire
456	STOP questionnaire
456	Snoring, Tiredness during daytime, Observed apnea, and high blood Pressure
457	CAMS-R 10-item version
457	Cognitive and Affective Mindfulness Scale - Revised 10-item version
458	SRRS
458	Social Readjustment Rating Scale
459	OCS
459	Obsession with COVID-19 Scale
460	IES-COVID19

460	Impact of Event Scale With Modifications for COVID-19
461	WHODAS
461	WHO Disability Assessment Schedule
462	XI
462	Xerostomia Inventory
463	BFI-10
463	Big Five 10
464	PCTQ
464	Perceived Coronavirus Threat Questionnaire
465	SLEQOL
465	Systemic Lupus Erythematosus-Specific Quality-Of-Life scale
466	SAWS
466	Satisfaction with Abilities and Well-being Scale
467	CPAQ-R
467	Chronic Pain Acceptance Questionnaire - Revised
468	CTS-PROMs Questionnaire/Severity Scale
468	Carpal Tunnel Patient Reported Outcomes Questionnaire
469	CQR
469	Compliance-Questionnaire-Rheumatology
470	CASQ
470	Combined Ankylosing Spondylitis Questionnaire
471	CODI
471	Combined Dimensions Index
472	MHI-5
472	Medical Outcomes Study 5-item Mental Health Index
473	FAOS
473	Foot and Ankle Outcome Score
474	HOOS
474	Hip disability and Osteoarthritis Outcome Score
475	NVSA
475	Nausea/Vomiting Symptom Assessment

476	PAMSI
476	Patient Assessment of Multiple Sclerosis Impact
477	KQoL-26
477	Knee Quality of Life
478	LPDS
478	Leuven Postprandial Distress Scale
479	HED
479	Hypogonadism Energy Diary
480	SQOR-V
480	Specific Quality of Life & Outcome Response - Venous
481	MPN-SAF TSS
481	MyeloProliferative Neoplasm Symptom Assessment Form Total Symptom Score
482	NPQ-SF
482	Neuropathic Pain Questionnaire - Short-form
483	NPQ
483	Neuropathic Pain Questionnaire
484	MESS
484	Milford Epworth Sleepiness Scale
485	MSQ
485	Motivational Structure Questionnaire
486	ICQ
486	Intermittent Claudication Questionnaire
487	Block Sodium Screener
487	Block Sodium Screener
488	Block Sugar Screener
488	Block Sugar Screener
489	EORTC QLQ-NHL-HG29
489	EORTC Quality of Life Questionnaire - Non Hodgkin Lymphoma High Grade Module
490	SALSA
490	Screening of Activity Limitation & Safety Awareness Questionnaire
491	PHQ-4

491	Patient Health Questionnaire-4 items
492	DRKA
492	Diabetic Retinopathy Knowledge and Attitudes
493	CARAT
493	Control of Allergic Rhinitis and Asthma Test
494	CUPP
494	Chronic Urticaria Patient Perspective
495	Sense of Coherence Scale
496	RAOS
496	Rheumatoid and Arthritis Outcome Score
497	Child's Version-PRQL
497	Child's Version-Pediatric Rheumatology Quality of Life Scale
498	Qualisex
498	Qualisex
499	HF-QoL
499	Hand-Foot Skin Reaction and Quality of Life questionnaire
500	RAI
500	Rheumatology Attitudes Index
501	ASD
501	Asthma Symptom Diary
502	SAQ
502	Scleroderma Assessment Questionnaire
503	MSQ
503	Medication Satisfaction Questionnaire
504	PDI
504	Pain Disability Index
505	PPAQ
505	Patient Perspective of Arrhythmia Questionnaire
506	NSP
506	Neuropathy Symptom Profile
507	Block 2000-Brief

507	Block Brief 2000 Food Frequency Questionnaire
508	Block 2005.1_PATH
508	Block 2005.1_PATH - Block 2005 Food Frequency Questionnaire – Asian American
509	MSIOA
509	Multiple Sclerosis Individual Outcome Assessment
510	SPI
510	Sleep Problems Index
511	CHES
511	COVID-19 Household Environment Scale
512	FCFI
512	Fear of COVID-19 Familial Infection Scale
513	PHQ-8
513	Patient Health Questionnaire-8 items
514	COV19-QoL
514	COVID-19–Impact on Quality of Life scale
515	CAS
515	Coronavirus Anxiety Scale
516	CRBS
516	Coronavirus Reassurance-Seeking Behaviors Scale
517	TAQ
517	Treatment Attitudes Questionnaire
518	SSS
518	Stanford Sleepiness Scale
519	GRCQ-S
519	Governmental Response to Coronavirus Questionnaire-Short
520	FGRCQ
520	Federal Governmental Response to Coronavirus Questionnaire
521	SGRCQ
521	State Governmental Response to Coronavirus Questionnaire
522	CGRCQ
522	City Governmental Response to Coronavirus Questionnaire

523	CEQ-S
523	Coronavirus Experiences Questionnaire-Short
524	CEQ
524	Coronavirus Experiences Questionnaire
525	PCTQ-S
525	Perceived Coronavirus Threat Questionnaire-Short
526	CIQ-S
526	Coronavirus Impacts Questionnaire-Short
527	CIQ
527	Coronavirus Impacts Questionnaire
528	CFS or CFQ
528	Chalder Fatigue Scale
529	IVI-CAT
529	IVI-CAT
530	ENS6Q
530	Empty Nose Syndrome 6-Item Questionnaire
531	FAAM
531	Foot and Ankle Ability Measure
532	MyPOS
532	Myeloma Patient Outcome Scale
533	iHOT-12
533	Short version of the International Hip Outcome Tool
534	PANQOL
534	Penn Acoustic Neuroma Quality-of-Life scale
535	MHQ
535	Michigan Hand Outcomes Questionnaire
536	QWLQ-CS
536	Quality of Working Life Questionnaire for Cancer Survivors
537	QoLHYPO
537	QoLHYPO
538	NeckPix

538	NeckPix
539	SAID
539	Sexual Arousal, Interest, and Drive Scale
540	ABCD
540	Assessment of Body Change and Distress questionnaire
541	Standardized Patient Evaluation of Eye Dryness
542	SAIQ
542	Self-Appraisal of Illness Questionnaire
543	Block FVF Screener
543	Block Fruit/Vegetable/Fiber Screener
544	EORTC- QLQ-NHL-LG20
544	EORTC Quality of Life Questionnaire - Non Hodgkin Lymphoma Low Grade Module
545	SDQ
545	Sleep Disorders Questionnaire
546	L-IPF Impacts
546	Living with Idiopathic Pulmonary Fibrosis (L-IPF) Impacts Questionnaire
547	K-BILD
547	King’s Brief Interstitial Lung Disease Questionnaire
548	PCS-C
548	Pain Catastrophizing Scale - Child version
549	DQOLY-SF
549	Diabetes Quality of Life for Youth scale - Short Form
550	PCFS
550	Post-COVID-19 Functional Status scale
551	TSK
551	Tampa Scale of Kinesiophobia
552	PBCS
552	Protective Behaviors towards COVID-19 Scale
553	CIAS
553	COVID-19 Induced Anxiety Scale
554	CRKS

554	COVID-19 Related Knowledge Scale
555	ABILHAND
555	ABILHAND
556	WPAI:SHP
556	Work Productivity and Activity Impairment Questionnaire: Specific Health Problem V2.0
557	VERITAS-PRN
557	Validated Hemophilia Regimen Treatment Adherence Scale – On-Demand
558	PRO-CTCAE
558	Patient-Reported Outcomes – Common Terminology Criteria for Adverse Events
559	DMS
559	Depressive Mood Scale
560	HDI
560	Headache Disability Inventory
561	HDQ
561	Headache-specific Disability Questionnaire
562	LAEP
562	Liverpool Adverse Events Profile
563	ePAQ - PO
563	electronic Personal Assessment Questionnaire - Pre-Operative
564	NOOS
564	Neck Outcome Score
565	HAGOS
565	Copenhagen Hip and Groin Outcome Score
566	ABC scale
566	Activities-Specific Balance Confidence Scale
567	QQ Method
567	Quantity and Quality Method
568	Raynaud’s Condition Score (RCS)
568	Raynaud’s Condition Score
569	RASE
569	Rheumatoid Arthritis Self Efficacy Scale

570	RADL
570	Resumption of Activities of Daily Living
571	RLDQ
571	Revised Leeds Disability Questionnaire
572	SST
572	Simple Shoulder Test
573	IBD-Control
573	Inflammatory Bowel Disease Control Questionnaire
574	iHOT-33
574	International Hip Outcome Tool
575	MSQPT
575	Multiple Sclerosis Questionnaire for Physical Therapists
576	PFIQ-7
576	Pelvic Floor Impact Questionnaire-7
577	PRAISE
577	Pulmonary Rehabilitation Adapted Index of Self-Efficacy
578	HeRQoLED-S
578	Health-Related Quality of Life for Eating Disorders questionnaire - Short form
579	SAT
579	Sarcoidosis Assessment Tool
580	M-ISI
580	Michigan Incontinence Symptom Index
581	saSPI
581	Self-Assessed Simplified Psoriasis Index
582	ShortMAC
582	Shortened (12-item) version of the Western Ontario and McMaster Universities Arthritis Index
583	SANE
583	Single Assessment Numeric Evaluation
584	PSEQ
584	Pain Self-Efficacy Questionnaire
585	PSEQ-2

585	2-item Pain Self-Efficacy Questionnaire
586	AOS
586	Ankle Osteoarthritis Scale
587	UPDD
587	Urticaria Patient Daily Diary
588	U-AIM
588	Urticaria Activity and Impact Measure
589	GBI
589	General Behavior Inventory
590	PoRI
590	Post-Operative Recovery Index
591	MMQL - Adolescent Form
591	Minneapolis-Manchester Quality of Life instrument - Adolescent Form
592	MMQL - Adult Form
592	Minneapolis-Manchester Quality of Life instrument - Adult Form
593	SMAIS-ULM
593	Spinal Muscular Atrophy Independence Scale Upper Limb Module
594	COVID-19-Related Symptoms Assessment
594	COVID-19-Related Symptoms Assessment
595	SSQ
595	Seizure Severity Questionnaire
596	GHIQ
596	Growth Hormone Injection Questionnaire
597	IVI-RC
597	Impact of Vision Impairment for Residential Care
598	PN-QOL
598	Peripheral Neuropathy Quality-of-Life instrument
599	RetCAT
599	Diabetic RETinopathy Computerized Adaptive Testing system
600	CTS-PROMs Questionnaire/Diagnosis
600	Carpal Tunnel Patient Reported Outcomes Questionnaire

601	ICF-Checklist
601	International Classification of Functioning, Disability and Health Checklist
602	KTQ-25
602	Kidney Transplant Questionnaire - 25-items
603	TCS
603	Tubiana and Chamagne Score
604	ePAQ - MPH
604	electronic Personal Assessment Questionnaire - Menstrual, Pain and Hormonal
605	ePAQ - PF
605	electronic Personal Assessment Questionnaire - Pelvic Floor
606	PEM
606	Patient Evaluation Measure
607	HCV-PRO
607	Hepatitis C Virus Patient-Reported Outcomes
608	SBI
608	Symptom Burden Index
609	HOS
609	Hip Outcome Score
610	EORTC QLQ-C15-PAL
610	EORTC Quality of Life Questionnaire - PALliative Cancer Care
611	SGRQ-I
611	St George’s Respiratory Questionnaire for Idiopathic Pulmonary Fibrosis
612	CPFQ
612	Cognitive and Physical Functioning Questionnaire
613	FOSQ-10
613	Functional Outcomes of Sleep Questionnaire Short Version
614	IPQS
614	Illness Perception Questionnaire for Schizophrenia
615	CARIFS
615	Canadian Acute Respiratory Illness and Flu Scale
616	SMST

616	Self-Management Self-Test
617	PainCAS
617	Pain Assessment Interview Network, Clinical Assessment System
618	GAIS
618	Global Aesthetic Improvement Scale
619	FCV-19S
619	Fear of COVID-19 Scale
620	ALSSQOL
620	Amyotrophic Lateral Sclerosis Specific Quality of Life
621	ALSSQOL-R
621	Amyotrophic Lateral Sclerosis Specific Quality of Life-Revised
622	BASQID
622	Bath Assessment of Subjective Quality of Life in Dementia
623	ADSD v1.0
623	Asthma Daytime Symptom Diary v1.0
624	GlauCAT
624	Glaucoma Computer Adaptive Test
625	ITAQ
625	Insight and Treatment Attitudes Questionnaire
626	LEAPS
626	Lam Employment Absence and Productivity Scale
627	CDQ-24
627	Craniocervical Dystonia Questionnaire
628	DRI
628	Disability Rating Index
629	PDAS
629	Patient-based Disease Activity Score
630	PGI-AS
630	Patient Generated Index for Ankylosing Spondylitis
631	FSS
631	Functional Shoulder Score

632	SPADI
632	Shoulder Pain and Disability Index
633	FS
633	Scleroderma Functional Score
634	HeRQoLEDv2
634	Health-Related Quality of Life for Eating Disorders questionnaire version-2
635	KOOS-PS
635	Knee injury and Osteoarthritis Outcome Score-Physical Function Short form
636	PFIQ
636	Pelvic Floor Impact Questionnaire
637	LIDAS
637	Limitations in Daily Activities Scale
638	VFQ-UI
638	Visual Function Questionnaire - Utility Index
639	OCS
639	Opioid Craving Scale
640	SDS
640	Severity of Dependence Scale
641	Mayers' LSQ (1), (2) and (3)
641	Mayers' Lifestyle Questionnaires (1), (2) and (3)
642	BrQ
642	Brace Questionnaire
643	PAGI-SYM
643	Patient Assessment of Gastrointestinal Disorders Symptom Severity Index
644	CANDID
644	Camberwell Assessment of Need for adults with Developmental and Intellectual Disabilities
645	QPD Panel
645	Quick PsychoDiagnostics Panel
646	ACQLI
646	Alzheimer's Carer's Quality of Life Instrument
647	Body Image Scale

648	Norfolk QOL-DN
648	Norfolk Quality of Life Questionnaire - Diabetic Neuropathy
649	heiQ
649	Health Education Impact Questionnaire
650	HNQ or MAPT
650	Hip and Knee Questionnaire
651	LFS or VAS-F
651	Lee Fatigue Scale
652	GCSI
652	Gastroparesis Cardinal Symptom Index
653	LQoL
653	Systemic Lupus Erythematosus Quality of Life Questionnaire
654	ORTHO BC-SAT
654	ORTHO Birth Control Satisfaction Assessment Tool
655	FSDS
655	Female Sexual Distress Scale
656	IPQ-R
656	Revised Illness Perception Questionnaire
657	ISL
657	Index of Sexual Life
658	SF-MPQ-2
658	Short-form McGill Pain Questionnaire
659	SATMED-Q
659	Treatment Satisfaction with Medicines Questionnaire
660	NDI
660	Nepean Dyspepsia Index
661	RAQoL
661	Rheumatoid Arthritis Quality of Life Questionnaire
662	SWAM Scale
662	Satisfaction With Antipsychotic Medication scale
663	AAQOL

663	Adolescent Asthma Quality of Life Questionnaire
664	DSIQ
664	Digestive Symptoms and Impact Questionnaire
665	A36 Hemofilia-QoL
665	Hemophilia-specific health-related quality of life questionnaire
666	4DSQ
666	Four-Dimensional Symptom Questionnaire
667	DTSQ-for-FIT20 Status and Change versions
667	Functional Insulin Treatment Satisfaction Questionnaire
668	PDQUALIF
668	Parkinson's Disease Quality of Life Scale
669	NV5
669	Osoba Nausea and Vomiting Module
670	MCSI
670	Multidimensional Caregiver Strain Index
671	INQoL
671	Individualized Neuromuscular Quality of Life Questionnaire
672	DAI-30
672	DAI-10
672	Drug Attitude Inventory
673	ILSS
673	Independent Living Skills Survey
674	Piers-Harris 2
674	Piers-Harris Children's Self-Concept Scale, Second Edition
675	CLDQ
675	Chronic Liver Disease Questionnaire
676	AQLQ-M
676	Asthma Quality of Life Questionnaire - Marks
677	QUAL HEMO
677	Haemophilia age group-specific Quality of life questionnaire
678	YQOL-FD

678	Youth Quality of Life Instrument - Facial differences Module
679	CAS
679	Caregiver Appraisal Scale
680	SOPA
680	Survey of Pain Attitudes
681	ADCPQ
681	Alzheimer's Disease Caregiver Preference Questionnaire
682	Camberwell Assessment of Need
683	PQAS and PQAS-R
683	Pain Quality Assessment Scale and Revised Pain Quality Assessment Scale
684	SAS-SR
684	Social Adjustment Scale - Self Report
685	PAR-ENT-QoL
685	Parents Questionnaire: The effects of Rhinopharyngitis and/or otitis of the child upon family life
686	NHP
686	Nottingham Health Profile
687	BSFQ
687	Brief Sexual Function Questionnaire
688	PsAQoL
688	Psoriatic Arthritis Quality of Life
689	CDIP-58
689	Cervical Dystonia Impact Profile
690	LDQ
690	Leeds Dyspepsia Questionnaire
691	Stoma-QOL
691	Stoma-QOL
692	LPSQ
692	Liverpool-PEG-Specific Questionnaire
693	FACIT-Sp-Non-Illness
693	Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being, a modified version for non-illness
694	IWQOL-Kids

694	Impact of Weight on Quality of Life - Kids
695	CDS
695	Carroll Rating Scale for Depression
696	VF-14
696	Visual Function Index
697	HBQOL
697	Heartburn-Specific Quality of Life Instrument
698	QOLM-P14
698	Quality of Life Module - Prostate 14
699	HSC
699	Herpes Symptom Checklist
700	PFQ
700	Psychosocial Functioning Questionnaire for Patients with Low Back Pain
701	ACT
701	Asthma Control Test
702	CECA
702	Cuestionario Específico en Condilomas Acuminados
703	SHIP
703	Studying the Hurdles of Insulin Prescription
704	WE-CARE
704	WEll-being and Satisfaction of CAREgivers of Children with Diabetes Questionnaire
705	FDLQI
705	Family Dermatology Life Quality Index
706	ARTS
706	OsteoARthritis Treatment Satisfaction Questionnaire
707	IPQ
707	Illness Perception Questionnaire
708	BASIS-24
708	Revised Behavior And Symptom Identification Scale
709	USP
709	Urinary Symptom Profile

710	WRSM
710	Weight-Related Symptom Measure
711	DSQL-CD
711	Dermatology-Specific Quality of Life instrument for Contact Dermatitis
712	PSIT
712	Patient Satisfaction with Insulin Therapy questionnaire
713	POEM
713	Patient-Oriented Eczema Measure
714	PAGI-QoL
714	Patient Assessment of Upper Gastrointestinal Disorders-Quality of Life
715	DAS59
715	Derriford Appearance Scale
716	PAC-QOL
716	Patient Assessment of Constipation Quality of Life questionnaire
717	SAQOL-39
717	Stroke and Aphasia Quality of Life Scale - 39 item version
718	QLSI
718	Quality of Life Systemic Inventory
719	WSFQ
719	Watts Sexual Function Questionnaire
720	FACIT-SP-Ex
720	Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being, Expanded version
721	SEAR
721	Self-Esteem and Relationship Questionnaire
722	Skindex
722	Skindex-29
722	Skindex-16
722	Skindex
723	PIMS
723	Parkinson's Impact Scale
724	SOS-10

724	Schwartz Outcome Scale-10
725	FSS
725	Fatigue Severity Scale
726	IND-VFQ
726	Indian Vision Function Questionnaire
727	BDI-II
727	Beck Depression Inventory - Second Edition
728	DEMQOL
728	Measurement of health-related quality of life for people with dementia
729	POQ
729	Prostate Outcomes Questionnaire
730	ICSQoL
730	International Continence Society-Benign Prostatic Hyperplasia study quality-of-life
731	DiabMedSat
731	Diabetes Medication Satisfaction
732	BASFI
732	Bath Ankylosing Spondylitis Functional Index
733	PEQ
733	Personal Experiences Questionnaire
734	BL-VAS
734	Bond-Lader VAS (Mood Rating Scale)
735	QUALIVEEN-30
735	QUALIVEEN 30 items
736	FIS
736	Fatigue Impact Scale
737	OSD
737	Ocular Surface Disease Questionnaire
738	MAF
738	Multidimensional Assessment of Fatigue
739	QOLRAD
739	Quality Of Life in Reflux And Dyspepsia

740	APPO-09
740	Attitudes Professionnelles des Pharmaciens d'Officine
741	EWPS
741	Endicott Work Productivity Scale
742	RGHQoL
742	Recurrent Genital Herpes Quality of Life Questionnaire
743	CAMPHOR
743	Cambridge Pulmonary Hypertension Outcome Review
744	PS-MS
744	Performance Scales for Multiple Sclerosis
745	Norfolk QOL-NET
745	Norfolk Quality of Life - Neuroendocrine Tumor Questionnaire
746	CDQ
746	Celiac Disease Questionnaire
747	VEINES-QOL
747	VEnous INsufficiency Epidemiological and Economic Study (VEINES) - Quality of Life
747	VEINES-Sym
747	VEnous INsufficiency Epidemiological and Economic Study (VEINES) - Symptoms
748	CROQ
748	Coronary Revascularisation Outcome Questionnaire
749	GSAS
749	Gastroesophageal Reflux Disease Symptom Assessment Scale
750	BASDAI
750	Bath Ankylosing Spondylitis Disease Activity Index
751	CTSQ
751	Cancer Therapy Satisfaction Questionnaire
752	AMS
752	Aging Males Symptoms Scale
753	CRQ-SAS
753	Chronic Respiratory Disease Questionnaire Self-Administered Standardized
754	DSM

754	Diabetes Symptom Measure
755	BREAST-Q
755	BREAST-Q
756	REPERES-60
756	REPERES-60
757	AI
757	Apathy Inventory
758	D-FIS
758	Daily Fatigue Impact Scale
759	GRID
759	Smoker Anchored Withdrawal Grid
760	PIQoL-AD
760	Parents' Index of Quality of Life in Atopic Dermatitis
761	LORQv3
761	Liverpool Oral Rehabilitation Questionnaire (version 3)
762	PAC-SYM
762	Patient Assessment of Constipation Symptoms
763	MSIS-29
763	Multiple Sclerosis Impact Scale
764	FACIT-SP
764	Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being
765	FACIT-SP-12
765	Functional Assessment of Chronic Illness Therapy - Spiritual Well-Being, The 12-item Spiritual Well-Being Scale
766	PTQL
766	Pictorial Thai Quality of Life
767	ULFI
767	Upper Limb Functional Index
768	PFSF
768	Profile of Female Sexual Function
769	MFIS
769	Modified Fatigue Impact Scale

770	SQLI
770	Stoma Quality of Life Index
771	QOL-E
771	Quality of Life E
772	SF-QUALIVEEN
772	QUALIVEEN Short Form
773	SRA
773	Subjects' Response to Antipsychotics
774	IMPACT III
774	IMPACT III
775	SCOPA-SLEEP
775	Scales for Outcomes in Parkinson’s Disease - Sleep Disturbances
776	DHP-18
776	Diabetes Health Profile
777	NPSI
777	Neuropathic Pain Symptom Inventory
778	DHSI
778	Digestive Health Status Instrument
779	AWQV2
779	Amphetamine Withdrawal Questionnaire Version 2
780	NA-ACP
780	Needs Assessment for Advanced Cancer Patients
781	SDI
781	Social Dysfunction Index
782	DAS24
782	Derriford Appearance Scale - Short form
783	CANE
783	Camberwell Assessment of Need for the Elderly
784	RLS-QoL or Hopkins RLS QoL
784	Restless Legs Quality of Life Scale or Hopkins RLS Quality of Life Scale
785	QUALIVEEN

785	QUALIVEEN
786	QLDS
786	Quality of Life in Depression Scale
787	QoLIAD
787	Quality of Life Index for Atopic Dermatitis
788	MSWS-12
788	Multiple Sclerosis Walking Scale
789	MSQoL
789	Migraine Specific Quality of Life Questionnaire
790	ZBI
790	Zarit Burden Interview
791	PDSS
791	Parkinson's Disease Sleep Scale
792	HOIQ
792	Herpes Outbreak Impact Questionnaire
793	NBD score
793	Neurogenic Bowel Dysfunction score
794	LFQ
794	Life Functioning Questionnaire
795	IDS-SR and IDS-C
795	Inventory of Depressive Symptomatology
796	ASQoL
796	Ankylosing Spondylitis Quality of Life Questionnaire
797	MHI
797	Mental Health Inventory
798	EDI-3
798	Eating Disorder Inventory
799	Wong-Baker FACES
799	Wong-Baker FACES Pain Rating Scale
800	SEQ Pain
800	Standard Evaluation Questionnaire on Pain

801	IFS
801	Iowa Fatigue Scale
802	FBA
802	Food Benefits Assessment
803	OWLQOL
803	Obesity and Weight-Loss Quality of Life measure
804	GlauQOL
804	Glaucoma Quality of Life Questionnaire
805	QUAL-E
805	Quality of Life at the End of Life Measure
806	IRLS
806	International Restless Legs Syndrome Study Group Rating Scale
807	MSHQ
807	Male Sexual Health Questionnaire
808	OFDQ
808	Osteoporosis Functional Disability Questionnaire
809	QUALIOST
809	QUAlity of Life questionnaire In OSTeoporosis
810	OPTQoL
810	Osteoporosis-Targeted Quality of Life Questionnaire
811	ICSmale
811	International Continence Society 'male'
812	TRIM-D Device
812	Treatment Related Impact Measure for Diabetes Device
813	CMDQ
813	Common Mental Disorder Questionnaire
814	DEBQ
814	Dutch Eating Behavior Questionnaire
815	NEMOQC
815	New Mother Quality of Care questionnaire
816	MAACL-R

816	Multiple Affect Adjective Checklist-Revised
817	DPM
817	Diabetes Productivity Measure
818	PRAC-Test
818	PRAgmatic Content and face validity Test
819	FIQ
819	Fibromyalgia Impact Questionnaire
820	FSHQ
820	Florida Sexual History Questionnaire
821	GHQ
821	General Health Questionnaire
822	GHSQ
822	Glasgow Health Status Questionnaires
823	DTSQs and DTSQc
823	Diabetes Treatment Satisfaction Questionnaire, status and change versions
824	DUFS
824	Dutch Fatigue Scale
825	DUSOCS
825	Duke Social Support and Stress Scale
826	ESI-55
826	Epilepsy Surgery Inventory
827	FLP
827	Functional Limitations Profile
828	GQOL
828	Global Quality of Life Scale
829	PQOL-12
829	12-Item Psoriasis Quality of Life Questionnaire
830	FSI
830	Fatigue Symptom Inventory
831	GHABP
831	Glasgow Hearing Aid Benefit Profile

832	GIVIO
832	GIVIO questionnaire
833	GLQ-8
833	GLQ-8
834	HADS
834	Hospital Anxiety and Depression Scale
835	DUKE-AD
835	Duke Anxiety - Depression Scale
836	ECQ
836	Edinburgh Claudication Questionnaire
837	FISI
837	Fecal Incontinence Severity Index
838	GSQ
838	General Satisfaction Questionnaire
839	HALex
839	Health and Activity Limitation Index
840	HAQUAMS
840	Hamburg Quality of Life Questionnaire Multiple Sclerosis
841	HDLF
841	Health and Daily Living Form
842	DUKE
842	Duke Health Profile
843	ECOS-16
843	Short Osteoporosis Quality of Life Questionnaire
844	FSQ
844	Functional Status Questionnaire
845	GSRS
845	Gastrointestinal Symptom Rating Scale - original interviewer-administered version
846	FIQL
846	Fecal Incontinence Quality of Life scale
847	GERD-HRQL

847	Gastroesophageal Reflux Disease Health Related Quality of Life scale
848	GIQLI
848	Gastrointestinal Quality of Life index
849	HAQ
849	Health Assessment Questionnaire
850	EQ-5D-3L
850	EuroQoL 5-Dimension 3-Level
851	FSAQ
851	Fallowfield's Sexual Activity Questionnaire
852	EDITS
852	Erectile Dysfunction Inventory of Treatment Satisfaction
853	ESAS-r
853	Edmonton Symptom Assessment System Revised
854	FACT-G
854	Functional Assessment of Cancer Therapy - General
855	FLIC
855	Functional Living Index: Cancer
856	FSFI
856	Female Sexual Function Index
857	GSRS-self
857	Gastrointestinal Symptom Rating Scale - self-administered version
858	HAT-QoL
858	HIV/AIDS-Targeted Quality of Life
859	HFS
859	Hypoglycemia Fear Survey or Adult Low Blood Sugar Survey
860	Brief IPQ
860	Brief Illness Perception Questionnaire
861	RMDQ-24
861	Roland-Morris Disability Questionnaire - 24 items
862	EORTC QLQ-LC13
862	EORTC Quality of Life Questionnaire - Lung Cancer Module

863	EORTC QLQ-H&N35
863	EORTC Quality of life - Head and Neck Cancer Module
864	PACT-Q
864	Perception of Anticoagulant Treatment Questionnaire
865	FIQR
865	Revised Fibromyalgia Impact Questionnaire
866	MEMSI
866	Manchester Early Morning Symptoms Index
867	SAPS
867	Short Assessment of Patient Satisfaction
868	LupusPRO
868	Lupus Patient-Reported Outcome tool
869	Borg Dyspnea Scale
869	Borg CR10 Scale
870	NRQLQ
870	Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire
871	OES
871	Oxford Elbow Score
872	EORTC QLQ-OV28
872	EORTC Quality of Life Questionnaire - Ovarian Cancer Module
873	TBQ
873	Burden of Treatment Questionnaire
874	Nausea Questionnaire
874	Nausea Questionnaire
875	P-RLS-SS
875	Pediatric Restless Legs Syndrome Severity Scale
876	PCS
876	Pain Catastrophizing Scale
877	USS PROM
877	Urethral stricture surgery patient-reported outcome measure
878	NePIQoL

878	Neuropathic Pain Impact on Quality-of-Life Questionnaire
879	RUIS
879	Revised Urinary Incontinence Scale
880	ACCEPT
880	Chronic Treatment Acceptance Questionnaire
881	QBPDS
881	Quebec Back Pain Disability Scale
882	POMS-Bi
882	Profile of Mood States Bipolar Scale
883	OSS
883	Oxford Shoulder Score
884	CQLQ
884	Cough Quality of Life Questionnaire
885	EORTC QLQ-CX24
885	EORTC Quality of Life Questionnaire - Cervical Cancer Module
886	EDQLS
886	Eating Disorders Quality of Life Scale
887	HDQoL
887	Huntington's Disease health-related Quality of Life questionnaire
888	EORTC QLQ-HCC18
888	EORTC Quality of Life Questionnaire - Hepatocellular Carcinoma/Primary Liver Cancer Module
889	OHRQoL Hypodontia
889	Oral Health Related Quality of Life for patients with Hypodontia
890	EORTC QLQ-PR25
890	EORTC Quality of Life Questionnaire - Prostate Cancer Module
891	MOS Sleep
891	Medical Outcomes Study Sleep scale
892	DFS-SF
892	Diabetic Foot Ulcer Scale - Short Form
893	howRU
893	howRU

894	OHS
894	Oxford Hip Score
895	PI-ED
895	Paediatric Index of Emotional Distress
896	OKS
896	Oxford Knee Score
897	BHQ
897	Bronchial Hyperresponsiveness Questionnaire
898	ASEX
898	Arizona Sexual Experience Scale
899	PDSS-2
899	Parkinson’s Disease Sleep Scale 2
900	QSU
900	Questionnaire on Smoking Urge
901	RFIS
901	Revised Faecal Incontinence Scale
902	EORTC QLQ-BN20
902	EORTC Quality of Life Questionnaire - Brain Cancer Module
903	ACD
903	Asthma Control Diary
904	ICQ and ICQ-S
904	Inhaled Corticosteroid Questionnaire
905	Fibromyalgia Rapid Screening Tool
906	PedsQL Diabetes Module 3.0
906	Pediatric Quality of Life Inventory 3.0 Diabetes Module
907	OSIS
907	Oxford Shoulder Instability Score
908	AF-QOL18
908	Quality of Life questionnaire for Patients with Atrial Fibrillation
909	EORTC QLQ-MY20
909	EORTC Quality of Life Questionnaire - Multiple Myeloma Module

910	AM-PAC CAT
910	Boston University Activity Measure for Post Acute Care
911	ASRS
911	Augmentation Severity Rating Scale
912	RLCQ
912	Recent Life Changes Questionnaire
913	EORTC QLQ-BR23
913	EORTC Quality of Life Questionnaire - Breast Cancer Module
914	QIDS-SR and QIDS-C
914	Quick Inventory of Depressive Symptomatology
915	Acne-QoL
915	Acne Quality of Life Questionnaire
916	SDS
916	Sheehan Disability Scale
917	LLFI
917	Lower Limb Functional Index
918	Measure of Outcome in Ocular Disease
919	MFSAF
919	Myelofibrosis Symptom Assessment Form
920	EORTC QLQ-HDC29
920	EORTC Quality of Life Questionnaire - High-Dose Chemotherapy
921	APFQ
921	Australian Pelvic Floor Questionnaire
922	Working Styles Assessment
922	Working Styles Assessment
923	mVCM1
923	modified Vision-Related Quality of Life Core Measure
924	VQOL
924	Vision-related Quality of Life Questionnaire
925	NBQ
925	Neck Bournemouth Questionnaire

926	PEIS
926	Pandemic Emotional Impact Scale
927	SATIS-Stroke
927	SATIS-Stroke scale
928	Lifestyle related behaviour questionnaire
928	Lifestyle related behaviour questionnaire
929	SFI
929	Sciatica Frequency Index
930	EORTC PATSAT-33 (with supplementary PATSAT-7 module)
930	EORTC Quality Of Life Questionnaire - IN-PATSAT-33 (with supplementary OUT PATSAT-7 module)
931	SEFAS
931	Self-reported Foot and Ankle Score
932	Sex-Q
932	Sexual Experience Questionnaire
933	CRADI
933	Colorectal Anal Distress Inventory
934	LyQLI
934	Lymphedema Quality of Life Inventory
935	TSK-11
935	Tampa Scale for Kinesiophobia-11
936	TSK Heart
936	Tampa Scale for Kinesiophobia Heart
937	UIQ-7
937	Urinary Impact Questionnaire-7
938	CSS
938	COVID Stress Scales
939	Lifestyle-related Behaviour Questionnaire
939	Impact of COVID-19 on lifestyle-related behaviours: eating habits, activity and sleep behaviour Questionnaire
940	PRRS
940	Pandemic Risk and Reaction Scale
941	COVID-19-PTSD

941	COVID-19 Post-Traumatic Stress Disorder
942	Covid-19 - Cardiothoracic Trainees
942	Covid-19 Impact on Cardiothoracic Trainees Questionnaire
943	Covid-19 USPs Questionnaire
943	Covid-19 Universal Safety Precautions Questionnaire
944	DISABKIDS DCGM-37 - SR version
944	Chronic Generic Module - Long version - Self-reported version
945	DISABKIDS DCGM-12 - SR version
945	Chronic Generic Module – Short version - Self-reported version
946	AAQ-S
946	Acceptance and Action Questionnaire-Stigma
947	PAAQ
947	Parental Acceptance and Action Questionnaire
948	AAQ-US
948	Acceptance and Action Questionnaire-University Students
949	AAQ-ABI
949	Acceptance and Action Questionnaire—Acquired Brain Injury
950	PROMIS Pediatric Short Form v2.0 – Upper Extremity 8a
950	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v2.0 – Upper Extremity 8a
951	PROMIS Pediatric Bank v1.0 - Physical Activity
951	Patient-Reported Outcomes Measurement Information System Pediatric Bank v1.0 - Physical Activity
952	ASK-Performance
952	Activities Scale for Kids-Performance
953	GlauCAT - Economic Scale
953	Glaucoma Computer Adaptive Test - Economic Scale
954	GlauCAT - Social Scale
954	Glaucoma Computer Adaptive Test - Social Scale
955	RetCAT - Convenience Scale
955	Diabetic RETinopathy Computerized Adaptive Testing system - Convenience Scale
956	AAQ-OC

956	Acceptance and Action Questionnaire for Obsessions and Compulsions
957	AADQ
957	Acceptance and Action Diabetes Questionnaire
958	CVD-AAQ
958	Cardiovascular Disease Acceptance and Action Questionnaire
959	IKHOAM
959	Ibadan Knee/Hip Osteoarthritis Outcome Measure
960	GDSS
960	Glasgow Dyspepsia Severity Score
961	ROE
961	Rhinoplasty Outcomes Evaluation
962	PRP
962	Pictoral Representation of Pain
963	RMDQ-23
963	Roland-Morris Disability Questionnaire - 23-items
964	CRISIS - Youth Self-Report Current Version Follow-Up
964	CoRonavIruS health and Impact Survey - Youth Self-Report Current Version Follow-Up
965	VISA-P
965	Victorian Institute of Sport Assessment-Patellar Tendon questionnaire
966	CPAQ-A8
966	Chronic Pain Acceptance Questionnaire - Adolescent Short Form
967	CPAQ-A
967	Chronic Pain Acceptance Questionnaire - Adolescent
968	STAXI-2
968	State-Trait Anger Expression Inventory–2
969	STPI
969	State-Trait Personality Inventory
970	PROMIS Pediatric Bank v1.0 – Physical Stress Experiences
970	Patient-Reported Outcomes Measurement Information System Pediatric Bank v1.0 – Physical Stress Experiences
971	HWQ
971	Health and Work Questionnaire

972	HQWP
972	Health-related Quality-of-life and Work Productivity questionnaire
973	E-RS: IPF
973	Evaluating Respiratory Symptoms: Idiopathic Pulmonary Fibrosis
974	PROMIS Physical Functioning in Sarcopenia
974	Patient-Reported Outcomes Measurement Information System Physical Functioning in Sarcopenia
975	Sickle Cell Pain Diary
975	Sickle Cell Pain Diary
976	SMILEY-Child Report
976	Simple Measure of Impact of Lupus Erythematosus in Youngsters-Child Report
977	PROMIS Parent Proxy Short Form v1.0 – Meaning and Purpose 4a
977	Patient-Reported Outcomes Measurement Information System - Parent Proxy Short Form v1.0 – Meaning and Purpose 4a
978	PROMIS Parent Proxy Bank v1.0 – Meaning and Purpose
978	Patient-Reported Outcomes Measurement Information System - Parent Proxy Bank v1.0 – Meaning and Purpose
979	Self ISTH BAT
979	Self International Society on Thrombosis and Haemostasis/Scientific and Standardization Committee Bleeding Assessment Tool
980	FVQ PRO
980	Functional Vision Questionnaire Patient-Reported Outcomes
981	VQoL-C
981	Vision-related Quality of Life Questionnaire for Children
982	SOS-SAH
982	Questionnaire for the Screening of Symptoms in aneurysmal Subarachnoid Hemorrhage
983	VFQ-3oo7
983	Visual Function Questionnaire 3 out of 7
984	ADVS
984	Activities of Daily Vision Scale
985	VDA
985	Visual Disability Assessment
986	PROMIS SF v1.0 – Dyspnea-Severity 10a

986	Patient Reported Outcomes Measurement Information System Item Bank - Short Form v1.0 – Dyspnea-Severity 10a
987	PROMIS SF v1.0 – Dyspnea-Functional Limitations 5a
987	Patient-Reported Outcomes Measurement Information System Short-Form v1.0 – Dyspnea-Functional Limitations 5a
988	ReQoL
988	Recovering Quality of Life questionnaire
989	LTCQ
989	Long-Term Conditions Questionnaire
990	LTCQ-8
990	Long-Term Conditions Questionnaire-8
991	PREOS-PC
991	Patient Reported Experiences and Outcomes of Safety in Primary Care
992	HASMID-10
992	Health and Self-Management in Diabetes-10
993	OARS
993	Oxford Arthroplasty Early Recovery Score
994	OACS
994	Oxford Arthroplasty Early Change Score
995	eHIQ
995	e-Health Impact Questionnaire
996	Mental Health Checklist
996	MHCL
997	C-19RS
997	COVID-19 Rumination Scale
998	DEQS
998	Dry Eye-Related Quality-of-Life Score
999	AHI
999	Arthritis Helplessness Index
1000	GAQ
1000	Gout Assessment Questionnaire
1001	PozQoL

1001	PozQoL Scale
1002	POPIQ
1002	Pelvic Organ Prolapse Impact Questionnaire
1003	CRAIQ
1003	Colo-Rectal-Anal Impact Questionnaire
1004	POPDI-6
1004	Pelvic Organ Prolapse Distress Inventory-6
1005	POPIQ-7
1005	Pelvic Organ Prolapse Impact Questionnaire-7
1006	PROMIS Pediatric Short Form v1.0 - Strength Impact 8a
1006	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 - Strength Impact 8a
1007	CAS
1007	COVID-19 Anxiety Scale
1008	SASS-14
1008	Self-Care Activities Screening Scale
1009	Neuro-QoL Scale v1.1 - Pediatric Upper Extremity - Fine Motor, ADL
1009	Quality of Life in Neurological Disorders Scale v1.1 - Pediatric Upper Extremity - Fine Motor, ADL
1010	R-PAct
1010	Rasch-built Pompe-specific Activity scale
1011	RetCAT - Activity Limitation Scale
1011	Diabetic RETinopathy Computerized Adaptive Testing system - Activity Limitation Scale
1012	RetCAT - Lighting Scale
1012	Diabetic RETinopathy Computerized Adaptive Testing system - Lighting Scale
1013	AAQ-SA
1013	Acceptance and Action Questionnaire - Substance Abuse
1014	Modified Von Korff Scales
1014	Modified Von Korff Scales
1015	Low-Back SF-36 PF18
1015	Low-Back Short Form-36 Physical Functioning
1016	ELCSA
1016	Latin American and Caribbean Food Security Scale

1017	CRISIS - Adult Self-Report Current Version Baseline
1017	CoRonavIruS health and Impact Survey - Adult Self-Report Current Version Baseline
1018	CRISIS - Youth Self-Report Full-Version Follow-Up
1018	CoRonavIruS health and Impact Survey - Youth Self-Report Full-Version Follow-Up
1019	mMOS-SS
1019	modified Medical Outcomes Study Social Support Survey
1020	CPAQ
1020	Chronic Pain Acceptance Questionnaire
1021	VISA-A
1021	Victorian Institute of Sport Assessment-Achilles questionnaire
1022	MFSI-SF
1022	Multidimensional Fatigue Symptom Inventory - Short Form
1023	MYMOP2
1023	Measure Yourself Medical Outcome Profile - Revised version
1024	STAI-CH
1024	State-Trait Anxiety Inventory for Children
1025	CHAQ-CV
1025	Childhood Health Assessment Questionnaire - Child's Version
1026	EATA
1026	Ergonomic Assessment Tool for Arthritis
1027	HPQ
1027	World Health Organization Health and Work Performance Questionnaire
1028	HAQ II
1028	Health Assessment Questionnaire II
1029	TACQOL-CF
1029	TNO AZL Children's Quality of Life - Children Form
1030	PASE
1030	Parent's Arthritis Self-Efficacy Scale
1031	PROMs-AS
1031	Multi-Dimensional Patient Reported Outcome Measures Questionnaire for Ankylosing Spondylitis
1032	ORQ

1032	Occupational Role Questionnaire
1033	ATAQ-IPF
1033	A Tool to Assess Quality of Life in Idiopathic Pulmonary Fibrosis
1034	PICMI
1034	Pediatric Inflammatory Crohn’s MRE Index
1035	QUALITE-Pain
1035	QUALIfied for Therapeutic Evaluations of Pain
1036	TUMMY-CD Index
1036	TUMMY-Crohn's Disease Index
1037	PROMIS SF v1.0 - Fatigue 10a
1037	Patient Reported Outcomes Measurement Information System - Short Form - Fatigue 10a
1038	PROMIS Short Form v1.1 - Pain Interference 4a
1038	Patient-Reported Outcomes Measurement Information System - Short Form v1.1 - Pain Interference 4a
1039	VISA-G
1039	Victorian Institute of Sport Assessment greater trochanteric pain syndrome
1040	PROMIS Short Form v1.1 - Pain Interference 8a
1040	Patient-Reported Outcomes Measurement Information System - Short Form v1.1 - Pain Interference 8a
1041	AASIS
1041	Alopecia Areata Symptom Impact Scale
1042	PROMIS Bank v1.0 - Meaning and Purpose
1042	Patient-Reported Outcomes Measurement Information System - Bank v1.0 - Meaning and Purpose
1043	Catquest-9SF
1043	Catquest-9 Short Form
1044	VND-Q
1044	Vision and Night Driving Questionnaire
1045	Catquest
1045	Catquest
1046	WPAI: Alopecia Areata
1046	Work Productivity and Activity Impairment: Alopecia Areata
1047	OKS-APQ

1047	Oxford Knee Score - Activity and Participation Questionnaire
1048	DMD QoL-Self Report
1048	Duchenne Muscular Dystrophy Quality of Life Measure - Self Report
1049	BWAQ
1049	Binge-Watching Addiction Questionnaire
1050	DSMT-Q
1050	Diabetes Self Management Technology Questionnaire
1051	Distress Scale
1051	Distress Scale
1052	CSES-8
1052	8-item Caregiver Self-Efficacy Scale
1053	Self-applied Acute Stress Scale
1054	BACKILL
1054	Back Illness Pain and Disability Scale
1055	SUIP-R
1055	Self-Understanding of Interpersonal Patterns Scale
1056	CALPAS
1056	California Psychotherapy Alliance Scale
1057	CRQ
1057	Central Relationship Questionnaire
1058	L-IPF Symptoms
1058	Living with Idiopathic Pulmonary Fibrosis (L-IPF) Symptoms Questionnaire
1059	GASS-C
1059	Glasgow Antipsychotic Side-effect Scale for Clozapine
1060	SLE-FAMILY
1060	Systemic Lupus Erythematosus Questionnaire on Family Role Functioning
1061	TSQM II
1061	Treatment Satisfaction Questionnaire for Medication - version II
1062	FRI
1062	Functional Rating Index
1063	ESS

1063	Epistaxis Severity Score
1064	SA-EASI
1064	Self-Administered Eczema Area and Severity Index
1065	EQS
1065	Erection Quality Scale
1066	GIS
1066	Gout Impact Scale
1067	FFbH-R
1067	Hannover Functional Ability Questionnaire
1068	QOL-RIQ
1068	Quality-of-Life for Respiratory Illness Questionnaire
1069	RIQ-MON10
1069	Respiratory Illness Questionnaire-monitoring 10
1070	HIP Female
1070	HPV Impact Profile Female
1071	DM-SAT
1071	Diabetes Medication Satisfaction Questionnaire
1072	MWPLQ
1072	Migraine Work and Productivity Loss Questionnaire
1073	MQoL
1073	Migraine Quality of Life Questionnaire
1074	S-SECEL
1074	Swedish Self Evaluation of Communication Experiences after Laryngeal Cancer
1075	MAAS-5
1075	Mindful Attention Awareness Scale-5
1076	KAP Covid-19 - Dental Health Care Professionals
1076	Knowledge, Attitudes and Practices regarding COVID-19 among Dental Health Care Professionals
1077	SCOVID Scale
1077	Self-Care in COVID-19 Scale
1078	CPDI
1078	Covid-19 Peritraumatic Distress Index

1079	COVID-19-related Psychosocial Distress
1079	COVID-19-related Psychosocial Distress
1080	VAAS-12
1080	Voices Acceptance and Action Scale-12
1081	VAAS-31
1081	Voices Acceptance and Action Scale
1082	VAAS-9
1082	Voices Acceptance and Action Scale-9
1083	FMI-13
1083	Freiburg Mindfulness Inventory-13
1084	GlauCAT - Treatment Convenience Scale
1084	Glaucoma Computer Adaptive Test - Treatment Convenience Scale
1085	GlauCAT - General Convenience Scale
1085	Glaucoma Computer Adaptive Test - General Convenience Scale
1086	GlauCAT - Lighting Scale
1086	Glaucoma Computer Adaptive Test - Lighting Scale
1087	RetCAT - Emotional Scale
1087	Diabetic RETinopathy Computerized Adaptive Testing system - Emotional Scale
1088	RetCAT - Social Scale
1088	Diabetic RETinopathy Computerized Adaptive Testing system - Social Scale
1089	PEDI-PRO
1089	Pediatric Evaluation of Disability Inventory-Patient Reported Outcome
1090	Covid-Epilepsy Follow-Up Questionnaire
1090	Covid-Epilepsy Follow-Up Questionnaire
1091	Community Pharmacists' Response Preparedness during COVID-19 Questionnaire
1091	Community Pharmacists' Response Preparedness during COVID-19 Questionnaire
1092	Mini-OAKHQOL
1092	Osteoarthritis Knee and Hip Quality Of Life - Short Form
1093	SOSGOQ2.0
1093	Spine Oncology Study Group Outcomes Questionnaire 2.0
1094	SIQ

1094	Systemic Lupus Erythematosus Impact Questionnaire
1095	LSSD
1095	Lupus Symptom Severity Diary
1096	PBQ
1096	Pediatric Bleeding Questionnaire
1097	FVQ-CYP
1097	Functional Vision Questionnaire for Children and Young People
1098	TLMK
1098	Tübinger Lebensqualitätsfragebogen für Männer mit Kinderwunsch
1099	OxAFQ-C
1099	Oxford Ankle Foot Questionnaire for Children (and caregivers)
1100	L-PF Symptoms
1100	Living with Pulmonary Fibrosis (L-PF) Symptoms Questionnaire
1101	MAAQ
1101	Mathematics Attitudes and Anxiety Questionnaire
1102	CCSQ
1102	Chemotherapy Convenience and Satisfaction Questionnaire
1103	CORPD
1103	COVID-19 related psychological distress in healthy public
1104	COVID-19 Vaccine KAPC
1104	COVID-19 Vaccine Knowledge Attitude Practices and Concerns
1105	KCOVID-19
1105	Knowledge of COVID-19 tool
1106	PVFS scale
1106	Post-VTE Functional Status scale
1107	LAPMER
1107	Level of Activity in Profound/Severe Mental Retardation
1108	PRE-COVID-19
1108	Scale of Worry for Contagion of COVID-19
1109	CWS
1109	Cancer Worry Scale

1110	Epicovid-19 Questionnaire
1110	Covid-19 National Epidemiological Survey
1111	SARS Self-Efficacy Scale
1111	SARS Self-Efficacy Scale
1112	CIQ
1112	Community Integration Questionnaire
1113	WSF
1113	Workstyle Short Form
1114	CSOQ
1114	Cervical Spine Outcomes Questionnaire
1115	DKQ-24
1115	Diabetes Knowledge Questionnaire - 24 items
1116	PGQ
1116	Pelvic Girdle Questionnaire
1117	QoR-40
1117	Quality of Recovery-40
1118	CSD
1118	Cough Severity Diary
1119	PAD
1119	Pediatric Asthma Diary
1120	FIQ
1120	Flushing Impact Questionnaire
1121	EORTC IN-PATSAT32
1121	EORTC Quality Of Life Questionnaire - IN-PATSAT32
1122	SED
1122	Sexual Events Diary
1123	SRS-22
1123	Scoliosis Research Society-22 patient questionnaire
1124	DHQ
1124	Daily Hunger Questionnaire
1125	SRS-7

1125	Scoliosis Research Society-7
1126	TSK-F
1126	Tampa Scale of Kinesiophobia-Fatigue
1127	CRAIQ-7
1127	Colorectal-Anal Impact Questionnaire-7
1128	CLSS
1128	Core Lower Urinary Tract Symptom score
1129	DIBSS-C
1129	Diary for Irritable Bowel Syndrome Symptoms-Constipation
1130	CRISIS - Adult Self-Report Full Version Baseline
1130	CoRonavIruS health and Impact Survey - Adult Self-Report Full Version Baseline
1131	COVID-19 FQCMC
1131	COVID-19 Fears Questionnaire for Chronic Medical Conditions
1132	COVISTRESS
1132	COronaVIrus on your life and on your STRESS
1133	ASK-Capability
1133	Activities Scale for Kids-Capability
1134	GlauCAT - Ocular Comfort Symptoms Scale
1134	Glaucoma Computer Adaptive Test - Ocular Comfort Symptoms Scale
1135	GlauCAT - Activity Limitation Scale
1135	Glaucoma Computer Adaptive Test - Activity Limitation Scale
1136	GlauCAT - Visual Symptoms Scale
1136	Glaucoma Computer Adaptive Test - Visual Symptoms Scale
1137	RetCAT - Health Concerns Scale
1137	Diabetic RETinopathy Computerized Adaptive Testing system - Health Concerns Scale
1138	ENLIST ENL Severity Scale
1138	Erythema Nodosum Leprosum International Study Erythema Nodosum Leprosum Severity Scale
1139	APFQ - Self-administered
1139	Australian Pelvic Floor Questionnaire - Self-administered version
1140	CRISIS - Adult Self-Report Full Version Follow-Up
1140	CoRonavIruS health and Impact Survey - Adult Self-Report Full Version Follow-Up

1141	CRISIS - Youth Self-Report Current Version Baseline
1141	CoRonavIruS health and Impact Survey - Youth Self-Report Current Version Baseline
1142	CRISIS AFAR - Youth and Adult Self-Report Version Baseline
1142	CoRonavIruS health and Impact Survey Adapted for Autism and Related Neurodevelopmental conditions - Youth and Adult Self-Report Version Baseline
1143	VISA-H
1143	Victorian Institute of Sport Assessment-Proximal Hamstring Tendons questionnaire
1144	MYMOP
1144	Measure Yourself Medical Outcome Profile
1145	CPAQ-8
1145	Chronic Pain Acceptance Questionnaire-8
1146	PROMIS Pediatric Short Form v1.0 – Physical Stress Experiences 4a
1146	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 – Physical Stress Experiences 4a
1147	PROMIS Pediatric Short Form v1.0 - Physical Stress Experiences 8a
1147	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 - Physical Stress Experiences 8a
1148	PROM for paediatric CFS/ME
1148	Patient Reported Outcome Measure for paediatric with Chronic Fatigue Syndrome/ Myalgic Encephalopathy
1149	HAQ-S
1149	Health Assessment Questionnaire for the Spondyloarthropaties
1150	FOQSD
1150	Functional Outcomes Questionnaire for Spinal Disorders
1151	OAKHQOL
1151	Osteoarthritis Knee and Hip Quality Of Life
1152	MVAS
1152	Million Visual Analogue Score
1153	KCCQ-12
1153	Kansas City Cardiomyopathy Questionnaire-12
1154	FACT-Item GP5
1154	Functional Assessment of Cancer Therapy - Item GP5
1155	FACT-ICM

1155	Functional Assessment of Cancer Therapy – Immune Checkpoint Modulator
1156	FACT-G Caregiver
1156	Functional Assessment of Cancer Therapy - General - Caregiver
1157	WHO Risk Drinking Levels of Alcohol Consumption
1157	World Health Organization Risk Drinking Levels of Alcohol Consumption
1158	PROMIS Pediatric Short Form v1.0 – Family Relationships 4a
1158	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 – Family Relationships 4a
1159	PROMIS Short Form v1.1 - Pain Interference 6a
1159	Patient-Reported Outcomes Measurement Information System - Short Form v1.1 - Pain Interference 6a
1160	PROMIS Parent Proxy Short Form v2.0 - Pain Interference 8a
1160	Patient-Reported Outcomes Measurement Information System - Parent Proxy Short Form v2.0 - Pain Interference 8a
1161	PROMIS Parent Proxy Bank v2.0 - Pain Interference
1161	Patient-Reported Outcomes Measurement Information System - Parent Proxy Bank v2.0 - Pain Interference
1162	ISTH BAT
1162	International Society on Thrombosis and Haemostasis/Scientific and Standardization Committee Bleeding Assessment Tool
1163	EYE-Q
1163	Effects of Youngsters' Eyesight on Quality of Life
1164	V-FUCHS
1164	Visual Function and Corneal Health Status
1165	PROMIS SF v1.0 – Dyspnea-Severity 5a
1165	Patient Reported Outcomes Measurement Information System Item Bank - Short Form v1.0 – Dyspnea-Severity 5a
1166	Generation Z Nursing Students Questionnaire
1166	Generation Z Nursing Students Questionnaire
1167	OCS
1167	Oxford Cognitive Screen
1168	PGS
1168	Pandemic Grief Scale
1169	COVID-19 Awareness Among Healthcare Professionals

1169	Coronavirus Disease 2019 Awareness Among Healthcare Professionals
1170	K-AC
1170	Knowledge and Attitude Scale Toward COVID-19 Pandemic Breaking Transmission Chain
1171	KAP
1171	Rural Residents' Knowledge, Attitude and Practice for the Prevention and Control of COVID-19
1172	NSS-P
1172	Pediatric Narcolepsy Severity Scale
1173	CFTS
1173	Contagion Fear and Threat Scale
1174	SQDES
1174	Short Questionnaire for Dry Eye Syndrome
1175	AECT
1175	Angioedema Control Test
1176	SLAQ
1176	Systemic Lupus Activity Questionnaire
1177	SANDE
1177	Symptom Assessment in Dry Eye
1178	Accidental Bowel Leakage Evaluation
1179	CQR5
1179	Compliance-Questionnaire-Rheumatology - 5-item version
1180	TSQM-9
1180	Treatment Satisfaction Questionnaire for Medication - 9 items
1181	WDI
1181	Waddell Disability Index
1182	DHI
1182	Dysphagia Handicap Index
1183	DIP
1183	Disability and Impact Profile
1184	DHEQ
1184	Dentine Hypersensitivity Experience Questionnaire
1185	VCM1

1185	Vision-Related Quality of Life Core Measure
1186	DKQ-15
1186	Diabetes Knowledge Questionnaire - 15 items
1187	JOABPEQ
1187	Japanese Orthopedic Association Back Pain Evaluation Questionnaire
1188	KOS-ADLS
1188	Knee Outcome Survey-Activities of Daily Living Scale
1189	KPS or AKPS
1189	Kujala Patellofemoral Scale or Anterior Knee Pain Scale
1190	DRHS
1190	Dyspepsia-Related Health Scale
1191	LKS
1191	Lysholm Knee Score
1192	SRISS
1192	Sleep-Related Itch and Scratch Scale
1193	MSBQ
1193	Maine Seattle Back Questionnaire
1194	HTN BOS
1194	Hypertension Battery of Scales (reduced)
1195	CSSQ
1195	COVID-19 Student Stress Questionnaire
1196	KAP
1196	City Residents' Knowledge, Attitude and Practice for the Prevention and Control of COVID-19
1197	mCKRS
1197	modified Cincinnati Knee Rating System
1198	PEF-COVID19
1198	Physical exercise level before and during social isolation
1199	CDAS
1199	COVID-19 Anxiety Scale
1200	SBI
1200	Sciatica Bothersomeness Index

1201	EORTC QLQ-FA12
1201	EORTC Quality Of Life Questionnaire FA12
1202	HidroQOL
1202	Hyperhidrosis Quality of Life Index
1203	SUS
1203	System Usability Scale Questionnaire
1204	CRADI-8
1204	Colorectal-Anal Distress Inventory-8
1205	TSK-TMD
1205	Tampa Scale for Kinesiophobia for Temporomandibular Disorders
1206	UEFI
1206	Upper Extremity Functional Index
1207	UEFI-15
1207	Upper Extremity Functional Index-15
1208	WOMET
1208	Western Ontario Meniscal Evaluation Tool
1209	WORQ
1209	Work, Osteoarthritis or joint-Replacement Questionnaire
1210	PROMIS Pediatric Bank - Upper Extremity
1210	Patient-Reported Outcomes Measurement Information System Pediatric Bank - Upper Extremity
1211	MAL-14
1211	Motor Activity Log
1212	TOPIC-Q
1212	Oxford Psychological Investigation of Coronavirus questionnaire
1213	Olfactory Questionnaire
1213	Olfactory Questionnaire
1214	PROMIS Short Form v1.0 - Fatigue 7a
1214	Patient-Reported Outcomes Measurement Information System - Short Form v1.0 - Fatigue 7a
1215	Myositis Activity Profile
1216	PROMs-FM
1216	Multi-Dimensional Patient Reported Outcome Measures Questionnaire for Fibromyalgia

1217	LBPRS
1217	Low Back Pain Rating Scale
1218	PROMIS - Plus-HF
1218	Patient-Reported Outcomes Measurement Information System - Plus-Heart Failure
1219	LSQ
1219	Lupus Satisfaction Questionnaire
1220	SROE
1220	Skin Rejuvenation Outcomes Evaluation
1221	FOE
1221	Facelift Outcomes Evaluation
1222	BOE
1222	Blepharoplasty Outcomes Evaluation
1223	PROMIS Pediatric Bank v2.0 - Pain Interference
1223	Patient-Reported Outcomes Measurement Information System - Pediatric Bank v2.0 - Pain Interference
1224	PROMIS Pediatric Short Form v1.0 – Meaning and Purpose 4a
1224	Patient-Reported Outcomes Measurement Information System - Pediatric Short Form v1.0 – Meaning and Purpose 4a
1225	PROMIS Pediatric Short Form v1.0 – Meaning and Purpose 8a
1225	Patient-Reported Outcomes Measurement Information System - Pediatric Short Form v1.0 – Meaning and Purpose 8a
1226	PROMIS Short Form v1.0 - Meaning and Purpose 4a
1226	Patient-Reported Outcomes Measurement Information System - Short Form v1.0 - Meaning and Purpose 4a
1227	PROMIS Short Form v1.0 - Meaning and Purpose 8a
1227	Patient-Reported Outcomes Measurement Information System - Short Form v1.0 - Meaning and Purpose 8a
1228	PROMIS Short Form v1.0 - Meaning and Purpose 6a
1228	Patient-Reported Outcomes Measurement Information System - Short Form v1.0 - Meaning and Purpose 6a
1229	GDS-5
1229	Geriatric Depression Scale-5
1230	School Age Self-PBQ
1230	School Age Self-Pediatric Bleeding Questionnaire

1231	Self-PBQ
1231	Self-Administered Pediatric Bleeding Questionnaire
1232	Sramek Bleeding Score
1232	Sramek Bleeding Score
1233	SPBQ
1233	Self-Administered Pediatric Bleeding Questionnaire
1234	FVQ-YP
1234	Functional Vision Questionnaire for Young People
1235	FVQ-C
1235	Functional Vision Questionnaire for Children
1236	PNG-VS QoL
1236	Papua New Guinea Vision-Specific Quality of Life questionnaire
1237	ULV-VFQ
1237	Ultra-Low Vision Visual Functioning Questionnaire
1238	L-PF Impacts
1238	Living with Pulmonary Fibrosis (L-PF) Impacts Questionnaire
1239	MSK-HQ
1239	Versus Arthritis Musculoskeletal Health Questionnaire
1240	PROMIS SF v1.0 – Dyspnea-Functional Limitations 5b
1240	Patient-Reported Outcomes Measurement Information System Short-Form v1.0 – Dyspnea-Functional Limitations 5b
1241	Socio-Behavioural Questionnaire
1241	Socio-Behavioural Impact of COVID-19 on the General Population
1242	Prevention Practices Against COVID-19 in Health Care Workers Questionnaire
1242	Prevention Practices Against COVID-19 in Health Care Workers Questionnaire
1243	Long Covid IT
1243	Long Covid Impact Tool
1244	MAL-28
1244	Motor Activity Log - 28 items
1245	Long Covid ST
1245	Long Covid Symptom Tool
1246	WAI

1246	Working Alliance Inventory
1247	KOOS-PF
1247	Knee injury and Osteoarthritis Outcome Score-Patellofemoral subscale
1248	SLENQ
1248	Systemic Lupus Erythematosus Needs Questionnaire
1249	VASFIQ
1249	Visual Analogue Scale of the Fibromyalgia Impact Questionnaire
1250	CAIT
1250	Cumberland Ankle Instability Tool
1251	WPSI
1251	Work Productivity Short Inventory (Wellness Inventory)
1252	WRFQ 2.0
1252	Work Role Functioning Questionnaire 2.0
1253	PSFS
1253	Patient-Specific Functional Scale
1254	PRAFAB-Q
1254	Protection, Amount of urine loss, Frequency of UI, Adjustment, and Body or self-image related to the incontinence symptoms questionnaire
1255	ADSS
1255	Atopic Dermatitis Sleep Scale
1256	QoR-15
1256	Quality of Recovery-15
1257	QoR Score
1257	Quality of Recovery Score
1258	SIIS
1258	Scratch Intensity and Impact Scale
1259	ASQ
1259	Appetite/Satiety Questionnaire
1260	MHGQ
1260	Men's Hair Growth Questionnaire
1261	WAA-QoL
1261	Women's Androgenetic Alopecia Quality of Life Questionnaire

1262	DysDD
1262	Dysmenorrhea Daily Diary
1263	DDSI
1263	Dual Diagnosis Screening Instrument
1264	Pediatric BSFS
1264	Pediatric Bristol Stool Form Scale
1265	OA-QI v2
1265	OsteoArthritis Quality Indicator version 2
1266	rCSHQ-RA
1266	Revised Cedars-Sinai Health-Related Quality of Life for Rheumatoid Arthritis Instrument
1267	HS-QoL
1267	Hidradenitis Suppurativa-Quality of Life
1268	POPDI
1268	Pelvic Organ Prolapse Distress Inventory
1269	SSV
1269	Subjective Shoulder Value
1270	UIQ
1270	Urinary Impact Questionnaire
1271	OHQoL-UK
1271	UK Oral Health-Related Quality-of-Life Measure
1272	CASQ-FI
1272	Combined Ankylosing Spondylitis Questionnaire-Functional Impairment
1273	CASQ-QoL
1273	Combined Ankylosing Spondylitis Questionnaire-Quality of Life
1274	SISQ
1274	Societal Influences Survey Questionnaire
1275	PREPS
1275	Pandemic-Related Pregnancy Stress Scale
1276	CPDI-CF
1276	Covid-19 Peritraumatic Distress Index- Cystic Fibrosis
1277	FMI-14

1277	Freiburg Mindfulness Inventory-14
1278	6-PAQ
1278	Parental Acceptance Questionnaire-6
1279	AFQ-Y8
1279	Avoidance and Fusion Questionnaire for Youth- 8 items
1280	EJ-IRAP
1280	The Emotional Judgment Implicit Relational Assessment Procedure
1281	AAQH
1281	Acceptance and Action Questionnaire for Hoarding
1282	The Tacting of Function Scale
1283	PROMIS Pediatric Short Form v2.0 – Mobility 8a
1283	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v2.0 – Mobility 8a
1284	PROMIS Pediatric Short Form v1.0 - Strength Impact 4a
1284	Patient-Reported Outcomes Pediatric Short Form v1.0 - Strength Impact 4a
1285	PROMIS Pediatric Short Form v1.0 - Physical Activity 8a
1285	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 - Physical Activity 8a
1286	ACTIVLIM-Stroke
1286	Activity Limitation Questionnaire-Stroke
1287	RetCAT - Visual Symptoms Scale
1287	Diabetic RETinopathy Computerized Adaptive Testing system - Visual Symptoms Scale
1288	RetCAT - Driving Scale
1288	Diabetic RETinopathy Computerized Adaptive Testing system - Driving Scale
1289	WHOQOL-BREF
1289	World Health Organization Quality of Life assessment instrument
1290	PQ
1290	Perform Questionnaire
1291	Covid-Epilepsy Questionnaire
1291	Covid-Epilepsy Questionnaire
1292	DEBQ-C
1292	Dutch Eating Behavior Questionnaire - Child version

1293	CRISIS - Adult Self-Report Current Version Follow-Up
1293	CoRonavIruS health and Impact Survey - Adult Self-Report Current Version Follow-Up
1294	CRISIS - Youth Self-Report Full-Version Baseline
1294	CoRonavIruS health and Impact Survey - Youth Self-Report Full-Version Baseline
1295	COVID-19 KAP
1295	Knowledge, Attitudes, Practices and Information Needs During the COVID-19
1296	SSS or ZCQ
1296	Modified Swiss Spinal Stenosis Scale or Zurich Claudication Questionnaire
1297	OHIP-20
1297	Oral Health Impact Profile for Edentulous patients
1298	TAI
1298	Test Anxiety Inventory
1299	PROMIS Pediatric Bank v1.0 - Psychological Stress Experiences
1299	Patient-Reported Outcomes Measurement Information System Pediatric Bank v1.0 - Psychological Stress Experiences
1300	Flare Assessment in Rheumatoid Arthritis
1301	FHAQ
1301	Fibromyalgia Health Assessment Questionnaire
1302	ORQ
1302	Obstacles to Return-to-Work Questionnaire
1303	OPQ
1303	Osteoporosis Questionnaire
1304	PROMIS Pediatric Chronic Kidney Disease Short Form - Sleep Disturbance
1304	Patient-Reported Outcomes Measurement Information System Pediatric Chronic Kidney Disease Short Form - Sleep Disturbance
1305	PROMIS Item Bank v1.1 - Pain Interference
1305	Patient-Reported Outcomes Measurement Information System - Item Bank v1.1 - Pain Interference
1306	PROMIS Short Form v1.1 - Pain Interference 6b
1306	Patient-Reported Outcomes Measurement Information System - Short Form v1.1 - Pain Interference 6b
1307	PROMIS Pediatric Bank v1.0 – Meaning and Purpose
1307	Patient-Reported Outcomes Measurement Information System - Pediatric Bank v1.0 – Meaning and Purpose

1308	PODCI-Self Report
1308	Pediatric Outcomes Data Collection Instrument-Self Report
1309	CFAbd-Score
1309	Cystic Fibrosis Abdomen-score
1310	Menorrhagia-Specific Screening Tool
1310	Menorrhagia-Specific Screening Tool
1311	ESS
1311	Epistaxis Scoring System
1312	LUNSERS
1312	Liverpool University Neuroleptic Side Effect Rating Scale
1313	NDPOQ
1313	Nutrition and Dietetic Patient Outcomes Questionnaires
1314	CDAQ
1314	Coeliac Disease Assessment Questionnaire
1315	AES-S
1315	Apathy Evaluation Scale - Self-rated
1316	CCLS-9
1316	Caregiver COVID-19 Limitations Scale
1317	Impact of COVID-19 on the Psychosocial Functioning of Peripartum Women Questionnaire
1317	Impact of COVID-19 on the Psychosocial Functioning of Peripartum Women Questionnaire
1318	Smart Working questionnaire
1318	Smart Working questionnaire
1319	DHIsf
1319	Dizziness Handicap Inventory - Short form
1320	MINDFIM
1320	MINFIM
1321	DHEQ-15
1321	Dentine Hypersensitivity Experience Questionnaire-15
1322	PRAP
1322	Pain Response to Activity and Positioning
1323	C19-RehabNeS

1323	COVID-19 Rehabilitation Needs Survey
1324	IEQ-SF
1324	Injustice Experience Questionnaire - Short Form
1325	CHART and CHART-SF
1325	Craig Handicap Assessment and Reporting Technique and Craig Handicap Assessment and Reporting Technique - Short form
1326	SSSC
1326	Sensation Seeking Scale for Children
1327	AIS
1327	Athens Insomnia Scale
1328	ALCES
1328	Adolescent Life Change Events Scale
1329	PBI
1329	Peer Behavior Inventory
1330	JTCI
1330	Junior Temperament and Character Inventory
1331	ADFLQ
1331	Adolescent Drinking and Family Life Questionnaire
1332	7-PAR
1332	7-day Physical Activity Recall
1333	modified Lysholm Score
1333	modified Lysholm Score
1334	WLQ-SF
1334	Work Limitations Questionnaire - Short Form
1335	GAD-7
1335	Generalized Anxiety Disorder - 7
1336	CLDEQ-8
1336	Contact Lens Dry Eye Questionnaire - 8 items
1337	COMIAD
1337	Core Outcome Measures Index - Anxiety and Depression
1338	WRFQ-10 2.0
1338	Work Role Functioning Questionnaire-10 2.0

1339	WRFQ-5 2.0
1339	Work Role Functioning Questionnaire-5 2.0
1340	Personalized Dyspnea Intensity Goal
1340	Personalized Dyspnea Intensity Goal
1341	ESS-ALT
1341	Epworth Sleepiness Scale-Alternative Version
1342	ODS-S
1342	Renzi Obstructed Defecation Syndrome Score
1343	Mini-OQLQ
1343	Mini Osteoporosis Quality of Life Questionnaire
1344	OQLQ
1344	Osteoporosis Quality of Life Questionnaire
1345	M-MASRI
1345	Modified-Medication Adherence Self-Report Inventory
1346	MAAS-A
1346	Mindful Attention Awareness Scale-Adolescent
1347	DIBSS-M
1347	Diary for Irritable Bowel Syndrome Symptoms-Mixed
1348	DIBSS-D
1348	Diary for Irritable Bowel Syndrome Symptoms-Diarrhea
1349	PROMIS Pediatric Bank v2.0 - Mobility
1349	Patient-Reported Outcomes Measurement Information System - Pediatric Bank - Mobility
1350	PROMIS Pediatric Bank - Strength Impact
1350	Patient-Reported Outcomes Measurement Information System Pediatric Bank - Strength Impact
1351	COVID-19-SES
1351	COVID-19 Prevention, Recognition and Home-Management Self-Efficacy Scale
1352	WSSQ
1352	Weight Self-Stigma Questionnaire
1353	PROMIS Pediatric Short Form v1.0 - Physical Activity 4a
1353	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 - Physical Activity 4a
1354	ACTIVLIM

1354	Activity Limitations Questionnaire
1355	GlauCAT - Concerns Scale
1355	Glaucoma Computer Adaptive Test - Concerns Scale
1356	GlauCAT - Emotional Scale
1356	Glaucoma Computer Adaptive Test - Emotional Scale
1357	GlauCAT - Mobility Scale
1357	Glaucoma Computer Adaptive Test - Mobility Scale
1358	RetCAT - Mobility Scale
1358	Diabetic RETinopathy Computerized Adaptive Testing system - Mobility Scale
1359	RetCAT - Economic Scale
1359	Diabetic RETinopathy Computerized Adaptive Testing system - Economic Scale
1360	KAP Survey regarding PPE among health care workers for the prevention of COVID-19
1360	Knowledge, attitude and practice survey regarding personal protective equipment among health care workers for the prevention of COVID-19
1361	KAP Towards COVID-19 Public Health Preventive Measures
1361	Knowledge, Attitudes and Practices Towards COVID-19 Public Health Preventive Measures
1362	Supportive Attitude toward Epidemic Prevention Measures Scale
1362	Supportive Attitude toward Epidemic Prevention Measures Scale
1363	Epidemic Worry Scale
1363	Epidemic Worry Scale
1364	CRISIS AFAR - Youth and Adult Self-Report Version Follow-Up
1364	CoRonavIruS health and Impact Survey Adapted for Autism and Related Neurodevelopmental conditions - Youth and Adult Self-Report Version Follow-Up
1365	Synkinesis Assessment Questionnaire
1365	Synkinesis Assessment Questionnaire
1366	VR-12
1366	Veterans RAND 12-Item Health Survey
1367	Vaizey score
1367	Vaizey score
1368	OHIP-EDENT
1368	Oral Health Impact Profile for Edentulous
1369	FIQ

1369	Functional Index Questionnaire
1370	STAXI-2 C/A
1370	State-Trait Anger Expression Inventory-2 Child and Adolescent
1371	AHI-5 Helplessness
1371	Arthritis Helplessness Index – 5 items
1372	AHI-7 Internality
1372	Arthritis Helplessness Index – 7 items
1373	EASi-QoL
1373	Evaluation of Ankylosing Spondylitis Quality of Life
1374	PROMIS Pediatric Short Form v1.0 – Psychological Stress Experiences 8a
1374	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 – Psychological Stress Experiences 8a
1375	PROMIS Pediatric Short Form v1.0 – Psychological Stress Experiences 4a
1375	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 – Psychological Stress Experiences 4a
1376	Function and Symptom Questionnaire
1376	Function and Symptom Questionnaire
1377	EEsAI
1377	Eosinophilic Esophagitis Activity Index
1378	FAAQ
1378	Food Craving Acceptance and Action questionnaire
1379	MHISS
1379	Mouth Handicap in Systemic Sclerosis
1380	AOSpine PROST
1380	Patient Reported Outcome Spine Trauma
1381	PROMIS Pediatric Chronic Kidney Disease Short Form- Fatigue
1381	Patient-Reported Outcomes Measurement Information System Pediatric Chronic Kidney Disease Short Form- Fatigue
1382	ANMS GCSI-DD
1382	American Neurogastroenterology and Motility Society Gastroparesis Cardinal Symptom Index Daily Diary
1383	FDSD
1383	Functional Dyspepsia Symptom Diary

1384	FACT-MBIS
1384	FACT/McGill Body Image Scale – Head & Neck (FACT-MBIS)
1385	PROMIS Item Bank v1.0 - Dyspnea Severity
1385	Patient Reported Outcomes Measurement Information System Item Bank - Dyspnea Severity
1386	PROMIS Pediatric Short Form v1.0 – Family Relationships 8a
1386	Patient-Reported Outcomes Measurement Information System Pediatric Short Form v1.0 – Family Relationships 8a
1387	PROMIS Pediatric Bank v1.0 – Family Relationships
1387	Patient-Reported Outcomes Measurement Information System Pediatric Bank v1.0 – Family Relationships
1388	PROMIS Pediatric Short Form v2.0 - Pain Interference 8a
1388	Patient-Reported Outcomes Measurement Information System - Pediatric Short Form v2.0 - Pain Interference 8a
1389	ALSAQ-5
1389	Amyotrophic Lateral Sclerosis Assessment Scales - 5 items
1390	PROMIS Parent Proxy Short Form v1.0 – Meaning and Purpose 8a
1390	Patient-Reported Outcomes Measurement Information System - Parent Proxy Short Form v1.0 – Meaning and Purpose 8a
1391	GDS-15
1391	Geriatric Depression Scale-15
1392	ASD
1392	Asthma Symptom Diary
1393	CNFDS
1393	Copenhagen Neck Function Disability Scale
1394	PROMIS SF v1.0 – Dyspnea-Severity 5b
1394	Patient Reported Outcomes Measurement Information System Item Bank - Short Form v1.0 – Dyspnea-Severity 5b
1395	Ora Calibra Ocular Discomfort Scale
1395	Ora Calibra Ocular Discomfort Scale
1396	McMonnies Questionnaire
1396	McMonnies Questionnaire
1397	MLDL
1397	Munich Quality-of-life Dimension List
1398	LBOS

1398	Low Back Outcome Score
1399	C19P-S
1399	COVID-19 Phobia Scale
1400	OCLEI
1400	Online Classroom Learning Environment Inventory
1401	GCS-NH
1401	Professional Good Care Scale in Nursing Homes
1402	NASS LSO
1402	North American Spine Society Lumbar Spine Outcome
1403	BIS
1403	Balanced Inventory for Spinal disorders
1404	HAQ-I
1404	Helping Alliance Questionnaire
1405	SQ-ISHI
1405	Satisfaction Questionnaire with Intravenous or Subcutaneous Hemophilia Injection
1406	NSS-CT
1406	Narcolepsy Severity Scale for Clinical Trials
1407	SFS
1407	SARS Fear Scale
1408	A-LPQ
1408	Angle Labor Pain Questionnaire
1408	A-PPMRT
1408	Angle Pictorial Pain Mapping & Pain Ranking Tool
1409	RESQ-7
1409	Reflux Symptom Questionnaire, 7 day recall
1410	DRS
1410	Disability Rating Scale
1411	HSIA
1411	Hidradenitis Suppurativa Impact Assessment
1412	RESQ-eD
1412	Reflux Symptom Questionnaire e-Diary

1413	MASQ
1413	Morning Activity and Symptoms Questionnaire
1414	GSRS - IBS
1414	Gastrointestinal Symptom Rating Scale - Irritable Bowel Syndrome
1415	mSCQ
1415	modified Smoking Consequences Questionnaire
1416	SSS-V
1416	Zuckerman Sensation Seeking Scales - Form V
1417	UPPS-P - Impulsive Behavior scale
1417	Urgency, Perseverance, Premeditation and Sensation Seeking Impulsive Behavior Scale- P
1418	API
1418	Authoritative Parenting Index
1419	KSS
1419	Karolinska Sleepiness Scale
1420	RAP-Q
1420	Risk & Prevention Questionnaire-Revised
1421	MSI
1421	Minnesota Smoking Index
1422	PACS
1422	Parent-Adolescent Communication Scale
1423	FACT-Ga
1423	Functional Assessment of Cancer Therapy-Gastric
1424	IES-R
1424	Impact of Event Scale-Revised
1425	Caregiver WLQ
1425	Caregiver Work Limitations Questionnaire
1426	HONC
1426	The Hooked on Nicotine Checklist
1427	BWCS
1427	Bowel Control Scale
1428	HaemoPREF

1428	Patient Perception and Preference for Haemophilia Treatment
1429	AUDIT
1429	Alcohol Use Disorders Identification Test Questionnaire
1430	BLCS
1430	Bladder Control Scale
1431	RDQ
1431	Reflux Disease Questionnaire
1432	AFImpact
1432	Atrial Fibrillation Impact Questionnaire
1433	CDLM
1433	Capacity of Daily Living during the Morning
1434	RSES
1434	Rosenberg Self-Esteem Scale
1435	DES-SF
1435	Diabetes Empowerment Scale Short Form
1436	IKDC SKF
1436	International Knee Documentation Committee Subjective Knee Evaluation Form
1437	BASH
1437	Brief Acculturation Scale for Hispanics
1438	FACT-AntiA
1438	Functional Assessment of Cancer Therapy for patients receiving Anti-Angiogenesis therapy
1439	COMM
1439	Current Opioid Misuse Measure
1440	BCSS
1440	The Breathlessness, Cough and Sputum Scale
1441	MASQ
1441	Mood and Anxiety Symptom Questionnaire
1442	PROMIS-GI
1442	Patient-Reported Outcomes Measurement Information System Gastrointestinal Symptom Scales
1443	FOS-SF
1443	Family of Origin Scale - Short Form versions

1444	FACT-E
1444	Functional Assessment of Cancer Therapy-Esophageal
1445	CTS2
1445	Conflict Tactics Scale
1446	PSS-Fa
1446	Perceived Social Support from Family
1447	PACES
1447	Physical ACtivity Enjoyment Scale
1448	Close-Friend scale
1448	Close-Friend scale
1449	PMSIS
1449	PreMenstrual Symptoms Impact Survey
1450	AIS-6
1450	Asthma Impact Survey
1451	RIS-6
1451	Rhinitis Impact Survey
1452	FAACT
1452	Functional Assessment of Anorexia/CachexiaTreatment
1453	Flu-PRO
1453	InFLUenza Patient-Reported Outcome
1454	HSCL
1454	Hopkins Symptom Checklist
1455	HAQ-II-P
1455	Revised Helping Alliance Questionnaire-Patient
1456	VQoL-YP
1456	Vision-related Quality of Life Questionnaire for Young People
1457	ANSD v1.0
1457	Asthma Nighttime Symptom Diary v1.0
1458	QUEST
1458	Quality of Life in Essential Tremor
1459	BAVQ-R

1459	Beliefs About Voices Questionnaire-Revised
1460	SRS
1460	Surgical Recovery Score
1461	FRI
1461	Functional Recovery Index
1462	SRI
1462	Surgical Recovery Index
1463	BF-Diary
1463	Bowel Function Diary
1464	SIS
1464	Sleep Impact Scale
1465	BRAF-NRS
1465	Bristol Rheumatoid Arthritis Fatigue - Numerical Rating Scale
1466	BAS-G
1466	Bath Ankylosing Spondylitis Global score
1467	WPAI:Lupus
1467	Work Productivity and Activity Impairment: Lupus
1468	BICLA
1468	BILAG-based Combined Lupus Assessment
1469	SSC
1469	Systemic lupus erythematosus Symptom Checklist
1470	SPAI-18
1470	Social Phobia and Anxiety Inventory short version
1471	SDSCA
1471	Summary of Diabetes Self-Care Activities
1472	APPADL
1472	Ability to Perform Physical Activities of Daily Living
1473	Prochaska ‘Stage of Change’ Questionnaire
1473	Prochaska ‘Stage of Change’ Questionnaire
1474	FJS
1474	The Forgotten Joint Score

1475	PO-SCORAD
1475	Patient-Oriented SCORing Atopic Dermatitis
1476	SMFA
1476	Short Muskuloskeletal Function Assessment
1477	EPDS
1477	Edinburgh Postnatal Depression Scale
1478	BEMIB
1478	Brief Evaluation of Medication Influences and Beliefs
1479	BIS-11
1479	Barratt Impulsiveness Scale
1480	DMSRQ-SF
1480	Diabetes Medication System Rating Questionnaire-Short Form
1481	ICOAP
1481	Measure of Intermittent and Constant Osteoarthritis Pain
1482	ALDS
1482	Academic Medical Center Linear Disability Score
1483	AAS
1483	Angioedema Activity Score
1484	UCT
1484	Urticaria Control Test
1485	PGA of the method of pain control
1485	Patient Global Assessment of the method of pain control
1486	Nurse EOC
1486	Nurse Ease-Of-Care Questionnaire
1487	FACT-M
1487	Functional Assessment of Cancer Therapy - Melanoma
1488	LCSS-Meso
1488	Lung Cancer Symptom Scale-Mesothelioma
1489	RUD
1489	Resource Utilization in Dementia
1490	TRIM-W

1490	Treatment Related Impact Measure - Weight
1491	KTSND
1491	Kano Test for Social Nicotine Dependence
1492	INTU
1492	Impact of Nighttime Urination Questionnaire
1493	ADPKD-UIS
1493	Autosomal Dominant Polycystic Kidney Disease Urinary Impact Scale
1494	SFQ
1494	Sexual Function Questionnaire
1495	HSDD
1495	Hypoactive Sexual Desire Disorder
1496	QEQ
1496	Quality of Erection Questionnaire
1497	Well-BFQ
1497	Well-being related to Food questionnaire
1498	JVB
1498	Jan van Breemen functional scale
1499	DISABKIDS
1499	DISABKIDS
1500	QOTA
1500	Questionnaire on Odor, Taste and Appetite
1501	SOIT
1501	Scandinavian Odor-Identification Test
1502	LCADL
1502	London Chest Activity of Daily Living scale
1503	NEADL
1503	Nottingham Extended Activities of Daily Living
1504	ADS
1504	Alcohol Dependence Scale
1505	CAT
1505	COPD Assessment Test

1506	CPSS
1506	Chronic Pain Self-Efficacy Scale
1507	ABOUT—Perceived Risk
1507	ABOUT—Perceived Risk (formally Perceived Risk Instrument - PRI)
1508	JAS
1508	Jenkins Activity Survey
1509	PPIUS
1509	Patient Perception of Intensity of Urgency Scale
1510	PAVE
1510	Proximal Antecedents to Violent Episodes
1511	IW-SP
1511	Impact of Weight on Self-Perception
1512	PSSI-5
1512	Posttraumatic Stress Disorder Symptom Scale Interview for DSM-5
1513	SLDS-C
1513	Satisfaction with Life Domains Scale for Cancer
1514	SLDS-BC
1514	Satisfaction with Life Domains Scale for Breast Cancer
1515	BIBCQ
1515	Body Image after Breast Cancer Questionnaire
1516	BMQ
1516	Beliefs about Medicines Questionnaire
1517	APS-POQ-R
1517	Revised American Pain Society Patient Outcome Questionnaire
1518	IVI-C
1518	Impact of Vision Impairment for Children
1519	SHAPS
1519	Snaith-Hamilton Pleasure Scale
1520	LQ
1520	Lifestyle Questionnaire
1521	DBAS

1521	Dysfunctional Beliefs and Attitudes about Sleep
1522	MCD-SS
1522	Multicentric Castleman's Disease Symptom
1523	TQOLIT - v1
1523	Tobacco Quality Of Life Impact Tool - v1
1524	AOM-Diary
1524	Acute Otitis Media Symptoms Diary
1525	ÖMSQ
1525	Örebro Musculoskeletal Screening Questionnaire
1526	TRIM-AGHD
1526	Treatment Related Impact Measure - Adult Growth Hormone Deficiency
1527	PDQ
1527	Perceived Deficits Questionnaire
1528	ETDQ-7
1528	Eustachian Tube Dysfunction Questionnaire
1529	DSDS
1529	Diabetes Semantic Differential Scales
1530	RPS-DD
1530	Risk Perception Survey for Developing Diabetes
1531	PEDT
1531	Premature Ejaculation Diagnostic Tool
1532	EORTC QLQ-CIPN20
1532	EORTC Quality of Life - Chemotherapy-Induced Peripheral Neuropathy
1533	SQOL-M
1533	Sexual Quality of Life - Men
1534	QoLISSY
1534	Quality of Life in Short Stature Youth
1535	VQoL-CYP
1535	Vision-related Quality of Life Questionnaire for Children and Young People
1536	Short CDAI
1536	Shortened and Simplified Crohn's Disease Activity Index

1537	MDQ
1537	Mood Disorder Questionnaire
1538	Ascites Impact Measure
1539	PASE
1539	Physical Activity Scale for the Elderly
1540	BRAF-MDQ
1540	Bristol Rheumatoid Arthritis Fatigue-Multidimensional Questionnaire
1541	PDS
1541	Posttraumatic Diagnostic Scale
1542	SAPASI
1542	Self-Administered Psoriasis Area and Severity Index
1543	CDS
1543	Cigarette Dependence Scale
1544	MedTech20
1544	MedTech20 Questionnaire
1545	PSS-I and PSS-SR
1545	Posttraumatic Stress Disorder Symptom Scale: Interview and Self Report
1546	PDS-5
1546	Posttraumatic Diagnostic Scale for DSM-5
1547	DSMQ
1547	Diabetes Self-Management Questionnaire
1548	SCI-R
1548	Self-Care Inventory-Revised
1549	RAID
1549	Rheumatoid Arthritis Impact of Disease score
1550	MFA
1550	Muskuloskeletal Function Assessment
1551	RA-WIS
1551	Rheumatoid Arthritis Work Instability Scale
1552	BMCS
1552	Beliefs about Medication Compliance Scale

1553	BDCS
1553	Beliefs about Dietary Compliance Scale
1554	MDP
1554	Multidimensional Dyspnea Profile
1555	BCSS
1555	Body Concealment Scale for Scleroderma
1556	MYCaW
1556	Measure Yourself Concerns and Wellbeing
1557	SHAQ
1557	Scleroderma Health Assessment Questionnaire
1558	DBAS-16
1558	Dysfunctional Beliefs and Attitudes about Sleep - 16
1559	NCS
1559	Nurse Competence Scale
1560	LCQ
1560	Lifestyle Changes Questionnaire
1561	LLFI-10
1561	Lower Limb Functional Index-10
1562	TRIM-HYPO
1562	Treatment Related Impact Measure - Hypoglycaemic Events
1563	FSQ
1563	Flushing Symptom Questionnaire
1564	OHA-Q
1564	Oral Hypoglycemic Agent Questionnaire
1565	ADPKD-PDS
1565	Autosomal Dominant Polycystic Kidney Disease Pain and Discomfort Scale
1566	ASFQ
1566	Abbreviated Sexual Function Questionnaire
1567	FluiiQ
1567	Influenza Intensity and Impact Questionnaire
1568	RBDSQ

1568	REM Sleep Behavior Disorder Screening Questionnaire
1569	IIEF-5 or SHIM
1569	International Index of Erectile Function - 5 items or Sexual Health Inventory for Men
1570	SQOL-F
1570	Sexual Quality of Life - Female
1571	DFS-FIBRO
1571	Daily Diary of Fatigue Symptoms – Fibromyalgia
1572	SPIM
1572	Spinal Pain Independence Measure
1573	THYCA-QoL
1573	THYroid CANcer-Quality of Life
1574	WED
1574	Well-being Enquiry for Diabetics questionnaire
1575	CSI
1575	Caregiver Strain Index
1576	FDI
1576	The Functional Disability Inventory
1577	CALI
1577	Child Activity Limitations Interview
1578	OCDS
1578	Obsessive Compulsive Drinking Scale
1579	SADQ
1579	Severity of alcohol dependence questionnaire
1580	SPIN
1580	Social Phobia Inventory
1581	SPAI
1581	Social Phobia and Anxiety Inventory
1582	CWS-21
1582	Cigarette Withdrawal Scale
1583	PDSS-SR
1583	Panic Disorder Severity Scale- Self Report

1584	PDSS-C
1584	Panic Disorder Severity Scale for Children
1585	SPAI-C
1585	Social Phobia and Anxiety Inventory for Children
1586	SAT II
1586	Self-Assessment of Treatment Questionnaire
1587	FACE-Q
1587	FACE-Q
1588	FOG-Q
1588	Freezing of Gait Questionnaire
1589	DMSRQ
1589	Diabetes Medication System Rating Questionnaire
1590	VisQoL
1590	Vision and Quality of Life Index
1591	LARS
1591	Lille Apathy Rating Scale
1592	NPAD
1592	Neck Pain and Disability Scale
1593	MARS
1593	Medication Adherence Rating Scale
1594	MC-QoL
1594	Mastocytosis Quality of Life Questionnaire
1595	HemoLatin-QoL
1595	HemoLatin-QoL
1596	AE-QoL
1596	Angioedema Quality of Life Score
1597	BODY-Q
1597	BODY-Q
1598	Patient EOC
1598	Patient Ease-Of-Care Questionnaire
1599	SCQoL

1599	Smoking Cessation Quality of Life
1600	IOC v2
1600	Impact of Cancer Version 2
1601	mFTQ
1601	modified Fagerstrom Tolerance Questionnaire
1602	AHLQ
1602	Adherence to a Healthy Lifestyle questionnaire (including Food Questionnaire module)
1603	iPCQ
1603	iMTA Productivity Cost Questionnaire
1604	ULFI-10
1604	Upper Limb Functional Index-10
1605	SFI-10
1605	Spine Functional Index-10
1606	PSI
1606	Psoriasis Symptom Inventory
1607	ADPKD-IS
1607	Autosomal Dominant Polycystic Kidney Disease Impact Scale
1608	PsAID
1608	Psoriatic Arthritis Impact of Disease
1609	HSSA
1609	Hidradenitis Suppurativa Symptom Assessment
1610	BPIC-SS
1610	Bladder Pain/Interstitial Cystitis Symptom Score
1611	PPBC
1611	Patient Perception of Bladder Condition
1612	SAGA
1612	Self-Assessment Goal Achievement questionnaire
1613	PD-Q
1613	painDETECT Questionnaire
1614	FSD
1614	Fibroid Symptom Diary

1615	EPBD
1615	Endometriosis Pain and Bleeding Diary
1616	ETSQ
1616	Endometriosis Treatment Satisfaction Questionnaire
1617	AUTOS
1617	Autonomy Over Smoking Scale
1618	GTQ
1618	Gothenburg Trismus Questionnaire
1619	NAIM
1619	Nasal Airflow Inducing Maneuver
1620	PIS
1620	Physical Impairment Scale
1621	PAS/PAS-II
1621	Patient Activity Scale
1622	FYPA
1622	Facilitators to Youth Physical Activity
1623	BYPA
1623	Barriers to Youth Physical Activity
1624	Back Pain Interference Scale
1624	Back Pain Interference Scale
1625	HIDRAdisk
1625	HIDRAdisk
1626	HSQoL-24
1626	Hidradenitis Suppurativa-Quality of Life Tool-24
1627	NoMoFA
1627	The Non-Motor Fluctuation Assessment Questionnaire
1628	PARS
1628	Postanaesthesia Recovery Score
1629	WOQ
1629	Wearing-off Questionnaire
1630	WSWS

1630	Wisconsin Smoking Withdrawal Scale
1631	COPM
1631	Canadian Occupational Performance Measure
1632	SWAL-QOL
1632	Swallowing Quality of Life questionnaire
1633	PLSI
1633	Psoriasis Life Stress Inventory
1634	LAI
1634	Lequesne's Algofunctional Index for Hip and Knee
1635	FACT-Taxane
1635	Functional Assessment of Cancer Therapy – Taxane
1636	DASS
1636	Depression Anxiety Stress Scales
1637	DASS-21
1637	Depression Anxiety Stress Scales Short Form
1638	BAI
1638	Beck Anxiety Inventory
1639	Mini-SPIN
1639	Social Phobia Inventory - Abbreviated Version
1640	AQ
1640	Autism Spectrum Quotient
1641	SNAS
1641	Sherbrooke Neuro-Oncology Assessment Scale
1642	PDSBE
1642	Physical Disability Sexual and Body Esteem
1643	KI
1643	Kupperman Index
1644	FACT-ES
1644	Functional Assessment of Cancer Therapy-Endocrine Subscale
1645	DFI
1645	Dyspnea-Fatigue Index

1646	RAQ
1646	Research Attitudes Questionnaire
1647	Starkstein Apathy Scale
1648	SQ
1648	Smoking Questionnaire
1649	PLD-Q
1649	Polycystic Liver Disease Questionnaire
1650	EPIC-CP
1650	Expanded Prostate Cancer Index Composite for Clinical Practice
1651	LQI
1651	Life Quality Index
1652	PT EOC
1652	Physical Therapist Ease-Of-Care Questionnaire
1653	SMWQ
1653	Study Medication Withdrawal Questionnaire
1654	ITEQ
1654	Insulin Treatment Experience Questionnaire
1655	Columbia Impairment Scale
1656	ÖMSQ-12
1656	Örebro Musculoskeletal Screening Questionnaire-12
1657	MAX-PC
1657	Memorial Anxiety Scale for Prostate Cancer
1658	A-OCDS
1658	Obsessive Compulsive Drinking Scale - Adolescent version
1659	BCPT
1659	Breast Cancer Prevention Trial Symptom Checklist
1660	BCTOS
1660	Breast Cancer Treatment Outcome Scale
1661	PedsQL Epilepsy Module
1661	Pediatric Quality of Life Inventory Epilepsy Module
1662	BSW

1662	Benefit, Satisfaction, and Willingness to Continue Treatment
1663	UPS
1663	Urgency Perception Scale
1664	EHS
1664	Erection Hardness Scale
1665	SCQ
1665	Schizophrenia Caregiver Questionnaire
1666	SSPRO
1666	Scleroderma Skin Patient Reported Outcome
1667	Strep-PRO
1667	Patient-Reported Symptom Scale for children with streptococcal pharyngitis
1668	PD-SAST
1668	Parkinson's Disease Sexual Addiction Screening Test
1669	SAC BDI-TDI
1669	Self-administered Computerized version of the BDI-TDI
1670	PedsQL Sickle Cell Disease Module
1670	Pediatric Quality of Life Inventory Sickle Cell Disease Module
1671	PedsQL Rheumatology Module
1671	Pediatric Quality of Life Inventory Rheumatology Module
1672	PedsQL Arthritis Module
1672	Pediatric Quality of Life Inventory Arthritis Module
1673	PedsQL Eosinophilic Esophagitis Symptoms Scales
1673	Pediatric Quality of Life Inventory Eosinophilic Esophagitis Symptoms Scales
1674	PedsQL Eosinophilic Esophagitis Module
1674	Pediatric Quality of Life Inventory Eosinophilic Esophagitis Module
1675	TNSS
1675	Total Nasal Symptom Score
1676	SFI
1676	Spine Functional Index
1677	FACT-L
1677	Functional Assessment of Cancer Therapy - Lung Cancer

1678	SEP
1678	Sexual Encounter Profile
1679	VAPI
1679	Vaccinees' Perception of Injection
1680	PedsQL
1680	Pediatric Quality of Life Inventory
1681	PedsQL End Stage Renal Disease Module
1681	Pediatric Quality of Life Inventory End Stage Renal Disease Module
1682	PedsQL Pediatric Pain Questionnaire
1682	Pediatric Quality of Life Inventory Pediatric Pain Questionnaire
1683	PedsQL Oral Health Scale
1683	Pediatric Quality of Life Inventory Oral Health Scale
1684	SIGH-SAD-SA
1684	Structured Interview Guide for the Hamilton Depression Rating Scale - Season Affective Disorder (Self-Assessment Version)
1685	TSQM 1.4
1685	Treatment Satisfaction Questionnaire for Medication - version 1.4
1686	PedsQL Stem Cell Transplant Module
1686	Pediatric Quality of Life Inventory Stem Cell Transplant Module
1687	TranQoL
1687	Transfusion-dependent QoL questionnaire
1688	FACT-P
1688	Functional Assessment of Cancer Therapy - Prostate Cancer
1689	SOS
1689	Service to Others in Sobriety
1690	Skindex-Teen
1690	Skindex-Teen
1691	SF-MPQ
1691	McGill Pain Questionnaire Short Form
1692	PedsQL Cognitive Functioning Scale
1692	Pediatric Quality of Life Inventory Cognitive Functioning Scale
1693	PedsQL Gastrointestinal Symptoms Module

1693	Pediatric Quality of Life Inventory Gastrointestinal Symptoms Module
1694	PedsQL Gastrointestinal Symptoms Scales
1694	Pediatric Quality of Life Inventory Gastrointestinal Symptoms Scales
1695	PedsQL Cardiac Module
1695	Pediatric Quality of Life Inventory Cardiac Module
1696	PedsQL Brain Tumor Module
1696	Pediatric Quality of Life Inventory Brain Tumor Module
1697	PedsQL General Well-Being Scale
1697	Pediatric Quality of Life Inventory General Well-Being Scale
1698	PedsQL Transplant Module
1698	Pediatric Quality of Life Inventory Transplant Module
1699	REFLETS
1699	REFlective evaLuation of psoriasis Efficacy of Treatment and Severity
1700	SIQR
1700	Revised Symptom Impact Questionnaire
1701	SFCI
1701	Swedish Fulminant Colitis Index
1702	FACT-An
1702	Functional Assessment of Cancer Therapy - Anemia
1703	EORTC QLQ-CR29
1703	EORTC Quality of Life Questionnaire - Colorectal Cancer Module
1704	TRIM-D
1704	Treatment Related Impact Measure for Diabetes
1705	ACTS
1705	Anti-Clot Treatment Scale
1706	PU-QOL
1706	Pressure Ulcer Quality of Life
1707	SPACE-Q
1707	Satisfaction of PAtients with Crohn's diseasE
1708	PedsQL Asthma Module Short Form
1708	Pediatric Quality of Life Inventory Asthma Module Short Form

1709	PedsQL Asthma Module
1709	Pediatric Quality of Life Inventory Asthma Module
1710	PedsQL Duchenne Muscular Dystrophy Module
1710	Pediatric Quality of Life Inventory Duchenne Muscular Dystrophy Module
1711	PedsQL Neurofibromatosis Module
1711	Pediatric Quality of Life Inventory Neurofibromatosis Module
1712	PedsQL Cerebral Palsy Module
1712	Pediatric Quality of Life Inventory Cerebral Palsy Module
1713	FACIT - SWIP
1713	Functional Assessment of Chronic Illness Therapy - Satisfaction with Pharmacist Scale
1714	BSFS
1714	Bristol Stool Form Scale
1715	RIBS
1715	Runco Ideational Behavior Scale
1716	FACT-BRM
1716	Functional Assessment of Cancer Therapy - Biologic Response Modifier
1717	FAMS-TOI
1717	Functional Assessment of Multiple Sclerosis: Trial Outcome Index
1718	FACIT-F
1718	Functional Assessment of Chronic Illness Therapy - Fatigue
1719	CNS-LS
1719	Center for Neurologic Study-Lability Scale
1720	OHQ
1720	Orthostatic Hypotension Questionnaire
1721	PedsQL Cancer Module
1721	Pediatric Quality of Life Inventory Cancer Module
1722	PedsQL Multidimensional Fatigue Scale
1722	Pediatric Quality of Life Inventory Multidimensional Fatigue Scale
1723	QuickDASH-9
1723	9-item version of the DASH (Disabilities of the Arm, Shoulder, and Hand)
1724	EORTC QLQ-BM22

1724	EORTC Quality of Life Questionnaire - Bone Metastases Module
1725	MusiQoL
1725	Multiple Sclerosis International Quality of Life questionnaire
1726	SOBQ
1726	The University of California, San Diego Shortness of Breath Questionnaire
1727	PedsQL Generic Core Scales Short Form 15
1727	Pediatric Quality of Life Inventory Generic Core Scales Short Form 15
1728	FACT-B
1728	Functional Assessment of Cancer Therapy - Breast Cancer
1729	HSQ
1729	Health Status Questionnaire 2.0
1730	IBCSG-QLC
1730	International Breast Cancer Study Group - Quality of Life Core Form
1731	IBQ
1731	Illness Behavior Questionnaire
1732	INV-2 and INVR
1732	Rhodes Index of Nausea and Vomiting-FORM 2 and Index of Nausea, Vomiting, and Retching
1733	ISS
1733	Influenza Symptom Severity scale
1734	KAS
1734	Katz Adjustment Scale (Epilepsy)
1735	KASE-AQ
1735	Knowledge, Attitude and Self-efficacy Asthma Questionnaire
1736	LSSS
1736	Liverpool Seizure Severity Scale
1737	MDASI
1737	MD Anderson Symptom Inventory
1738	MDQ
1738	Multidimensional Diabetes Questionnaire
1739	MIDAS
1739	Migraine Disability Assessment

1740	HQLI
1740	Hospice Quality of Life Index
1741	IBDQOL
1741	Inflammatory Bowel Disease Quality of Life Questionnaire
1742	IBS-36
1742	IBS-36
1743	IPS
1743	Integrated Pain Score
1744	ISI
1744	Incontinence Stress Index
1745	KHQ
1745	King's Health Questionnaire
1746	LQOLP
1746	Lancashire Quality of Life Profile
1747	IBDQ
1747	Inflammatory Bowel Disease Questionnaire
1748	IIWS
1748	Influenza Impact Wellbeing Scale
1749	KCCQ
1749	Kansas City Cardiomyopathy Questionnaire
1750	KOOS
1750	Knee Injury and Osteoarthritis Outcome Score
1751	LASA-S
1751	Linear Analogue Self-Assessment-Selby
1752	LHS
1752	London Handicap Scale
1753	LVQOL
1753	Low Vision Quality-of-Life Questionnaire
1754	MiniAQLQ
1754	Mini Asthma Quality of Life Questionnaire
1755	MiniRQLQ

1755	Mini Rhinoconjunctivitis Quality of Life Questionnaire
1756	HNQOL
1756	Head and Neck Quality of Life instrument
1757	HYPER 31
1757	Hypertension Health Status Inventory
1758	IIEF
1758	International Index of Erectile Function
1759	I-QOL
1759	Urinary Incontinence-Specific Quality of Life
1760	KINDL
1760	Revidierter KINDer Lebensqualitätsfragebogen
1761	LCSS
1761	Lung Cancer Symptom Scale
1762	LFUQ
1762	Leg and Foot Ulcer Questionnaire
1763	MACTAR
1763	McMaster Toronto Arthritis Patient Preference Disability Questionnaire
1764	MHLC
1764	Multidimensional Health Locus of Control Scales
1765	DIS
1765	Detrusor Instability Score
1766	HOPES
1766	HIV Overview of Problems - Evaluation System
1767	HUI
1767	Health Utilities Index
1768	IDS
1768	Illness Distress Scale
1769	IRE
1769	Indice de Resistencia a la Enfermedad [Resistance to Illness Index]
1770	LSAS
1770	Liebowitz Social Anxiety Scale

1771	LWAQ
1771	Living with Asthma Questionnaire
1772	MacNew
1772	MacNew Heart Disease Health-related Quality of Life Questionnaire
1773	MANE
1773	Morrow Assessment of Nausea and Emesis
1774	MFSI
1774	Multidimensional Fatigue Symptom Inventory
1775	EHP-30
1775	Endometriosis Health Profile-30
1776	IVI
1776	Impact of Vision Impairment
1777	MADRS
1777	Montgomery-Asberg Depression Rating Scale
1778	MHIQ
1778	McMaster Health Index Questionnaire
1779	MINICHAL
1779	Short form of Quality of Life Questionnaire for Arterial hypertension
1780	MLHF
1780	Minnesota Living with Heart Failure Questionnaire
1781	PSC PRO
1781	Primary Sclerosing Cholangitis - PRO
1782	SIBDQ
1782	Short Inflammatory Bowel Disease Questionnaire
1783	HAE PRO
1783	Hereditary Angioedema Patient Reported Outcomes
1784	NFBSI-16
1784	National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy-Breast Cancer Symptom Index
1785	HFRDIS
1785	Hot Flash Related Daily Interference Scale
1786	SCI-FI SFs

1786	Spinal Cord Injury–Functional Index short forms
1787	SCI-FI/AT
1787	Spinal Cord Injury - Functional Index/Assistive Technology
1788	NIH Toolbox - Parent Report Bank FF v2.0 - Positive Affect
1788	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Positive Affect
1789	NIH Toolbox - Parent Report Bank FF v2.0 - Fear
1789	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Fear
1790	NIH Toolbox - Parent Report Bank FF v2.0 - Anger
1790	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Anger
1791	NIH Toolbox - Parent Report Bank v2.0 - Anger
1791	NIH Toolbox - Parent Report Bank v2.0 - Anger
1792	NIH Toolbox - Parent Report Bank v2.0 - Fear
1792	NIH Toolbox - Parent Report Bank v2.0 - Fear
1793	NIH Toolbox - Bank FF v2.0 - Perceived Hostility
1793	NIH Toolbox - Bank Fixed Form v2.0 - Perceived Hostility
1794	NIH Toolbox - Bank v2.0 - Loneliness
1794	NIH Toolbox - Bank v2.0 - Loneliness
1795	NIH Toolbox - Bank v2.0 - Perceived Hostility
1795	NIH Toolbox - Bank v2.0 - Perceived Hostility
1796	NIH Toolbox - Bank FF v2.0 - Fear - Somatic Arousal
1796	NIH Toolbox - Bank Fixed Form v2.0 - Fear - Somatic Arousal
1797	NIH Toolbox - Bank FF v2.0 - Fear - Affect
1797	NIH Toolbox - Bank Fixed Form v2.0 - Fear - Affect
1798	NIH Toolbox - Bank v2.0 - Fear - Somatic Arousal
1798	NIH Toolbox - Bank v2.0 - Fear - Somatic Arousal
1799	NIH Toolbox - Bank v2.0 - Anger- Hostility
1799	NIH Toolbox - Bank v2.0 - Anger- Hostility
1800	NIH Toolbox - Bank v2.0 - Fear - Affect
1800	NIH Toolbox - Bank v2.0 - Fear - Affect
1801	NIH Toolbox - Bank FF v2.0 - Meaning and Purpose
1801	NIH Toolbox - Bank Fixed Form v2.0 - Meaning and Purpose

1802	NIH Toolbox - Bank FF v2.0 - Instrumental Support
1802	NIH Toolbox - Bank Fixed Form v2.0 - Instrumental Support
1803	NIH Toolbox - Bank v2.0 - Instrumental Support
1803	NIH Toolbox - Bank v2.0 - Instrumental Support
1804	NFBISI-18
1804	National Comprehensive Cancer Network Functional Assessment of Cancer Therapy - Bladder Symptom Index-18
1805	LCQ
1805	Leicester Cough Questionnaire
1806	Jarad Score
1806	Jarad and Sequeiros Symptom Score Questionnaire
1807	R-ODS
1807	Rasch-built Overall Disability Scale
1808	PROMIS Item Bank v. 1.0 – Emotional Distress - Depression
1808	Patient-Reported Outcomes Measurement Information System Item Bank v. 1.0 – Emotional Distress - Depression
1809	PROMIS Item Bank v1.0 – Smoking: Social Motivations for Nondaily Smokers
1809	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Social Motivations for Nondaily Smokers
1810	PROMIS Item Bank v1.0 – Smoking: Social Motivations for Daily Smokers
1810	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Social Motivations for Daily Smokers
1811	PROMIS Item Bank v.1.0 – Smoking: Social Motivations for All Smokers
1811	Patient-Reported Outcomes Measurement Information System Item Bank v.1.0 – Smoking: Social Motivations for All Smokers
1812	WPAI:ASTHMA
1812	Work Productivity and Activity Impairment Questionnaire: Asthma
1813	Resilience Supports Scale for Youth
1813	Resilience Supports Scale for Youth
1814	Resilience Assessment for Youth
1814	Resilience Assessment for Youth
1815	FPHPQ
1815	Fabry-specific Pediatric Health and Pain Questionnaire
1816	WPAI:LLF

1816	Work Productivity and Activity Impairment Questionnaire: Lower Limb Fracture
1817	WPAI:GOUT
1817	Work Productivity and Activity Impairment Questionnaire: Gout
1818	WPAI:ANS v2.0
1818	Work Productivity and Activity Impairment Questionnaire: Anemic Symptoms, Version 2.0
1819	WPAI:Axial Spondyloarthritis v2.0
1819	Work Productivity and Activity Impairment Questionnaire: Axial Spondyloarthritis, Version 2.0
1820	WPAI:DMD-CG
1820	Work Productivity and Activity Impairment Questionnaire: Duchenne Muscular Dystrophy, Caregiver Version 2.0
1821	CWBS
1821	Caregiver Well-Being Scale
1822	EARP
1822	Early Arthritis for Psoriatic Patients Questionnaire
1823	ETI-SR
1823	Early Trauma Inventory - Self Report
1824	SCI-FI
1824	Spinal Cord Injury - Functional Index
1825	SCI-FI/AT SFs
1825	Spinal Cord Injury - Functional Index/Assistive Technology Short Forms
1826	NIH Toolbox - Parent Report Bank FF v2.0 - Social Withdrawal
1826	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Social Withdrawal
1827	NIH Toolbox - Parent Report Bank v2.0 - Positive Affect
1827	NIH Toolbox - Parent Report Bank v2.0 - Positive Affect
1828	NIH Toolbox - Parent Report Bank v2.0 - Perceived Stress
1828	NIH Toolbox - Parent Report Bank v2.0 - Perceived Stress
1829	NIH Toolbox - Parent Report Bank v2.0 - General Life Satisfaction
1829	NIH Toolbox - Parent Report Bank v2.0 - General Life Satisfaction
1830	NIH Toolbox - Bank FF v2.0 - General Life Satisfaction
1830	NIH Toolbox - Bank Fixed Form v2.0 - General Life Satisfaction
1831	NIH Toolbox - Parent Report Bank v2.0 - Self-Efficacy
1831	NIH Toolbox - Parent Report Bank v2.0 - Self-Efficacy

1832	NIH Toolbox - Bank FF v2.0 - Perceived Rejection
1832	NIH Toolbox - Bank Fixed Form v2.0 - Perceived Rejection
1833	NIH Toolbox - Bank FF v2.0 - Sadness
1833	NIH Toolbox - Bank Fixed Form v2.0 - Sadness
1834	NIH Toolbox - Bank v2.0 - Perceived Rejection
1834	NIH Toolbox - Bank v2.0 - Perceived Rejection
1835	NIH Toolbox - Bank v2 0 - Meaning and Purpose
1835	NIH Toolbox - Bank v2 0 - Meaning and Purpose
1836	WPAI:GERD-SDQ
1836	Work Productivity and Activity Impairment: Gastro-Esophageal Reflux Disease, Sleep Disturbances Questionnaire
1837	NIH Toolbox - Negative Parent Relationship Survey
1837	NIH Toolbox - Negative Parent Relationship Survey
1838	NIH Toolbox - Sibling Rejection Survey
1838	NIH Toolbox - Sibling Rejection Survey
1839	FACT-Cx
1839	Functional Assessment of Cancer Therapy - Cervix
1840	I-TAQ
1840	Injection Treatment Acceptance Questionnaire
1841	PROMIS Item Bank v1.1 – Anger
1841	Patient-Reported Outcomes Measurement Information System Item Bank v1.1 – Anger
1842	PSS14
1842	Perceived Stress Scale 14 items
1843	PROMIS Item Bank v1.0 – Smoking: Emotional and Sensory Expectancies for Daily Smokers
1843	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Emotional and Sensory Expectancies for Daily Smokers
1844	PROMIS Item Bank v1.0 – Smoking: Emotional and Sensory Expectancies for Nondaily Smokers
1844	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Emotional and Sensory Expectancies for Nondaily Smokers
1845	PROMIS Item Bank v.1.0 – Smoking: Emotional and Sensory Expectancies for All Smokers
1845	Patient-Reported Outcomes Measurement Information System Item Bank v.1.0 – Smoking: Emotional and Sensory Expectancies for All Smokers
1846	PROMIS Item Bank v1.0 – Smoking: Coping Expectancies for Nondaily Smokers

1846	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Coping Expectancies for Nondaily Smokers
1847	WPAI:Hepatitis C
1847	Work Productivity and Activity Impairment Questionnaire: Hepatitis C
1848	NFOG-Q
1848	New Freezing of Gait Questionnaire
1849	WPAI:Uveitis v2.0
1849	Work Productivity and Activity Impairment Questionnaire: Uveitis, Version 2.0
1850	PROMIS SexFS Brief Profile v1.0 – Female
1850	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Brief Profile v1.0 – Female
1851	PROMIS SexFS Brief Profile v1.0 – Male
1851	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Brief Profile v1.0 – Male
1852	WPAI:AD v2.0
1852	Work Productivity and Activity Impairment Questionnaire: Atopic Dermatitis, Version 2.0
1853	NFHSI-18
1853	National Comprehensive Cancer Network Functional Assessment of Cancer Therapy - Hepatobiliary-Pancreatic Symptom Index
1854	CWBS-SF
1854	Caregiver Well-Being Scale - Short-form
1855	DUI
1855	Diabetes Utility Index
1856	HRUQ
1856	HealthCare Resource Utilization Questionnaire
1857	HFI
1857	Hot Flash Interference scale
1858	NIH Toolbox - Parent Report Bank FF v2.0 - Sadness
1858	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Sadness
1859	NIH Toolbox - Parent Report Bank v2.0 - Sadness
1859	NIH Toolbox - Parent Report Bank v2.0 - Sadness
1860	NIH Toolbox - Bank v2.0 - Fear
1860	NIH Toolbox - Bank v2.0 - Fear

1861	NIH Toolbox - Bank FF v2.0 - Fear
1861	NIH Toolbox - Bank Fixed Form v2.0 - Fear
1862	NIH Toolbox - Bank FF v2.0 - Loneliness
1862	NIH Toolbox - Bank Fixed Form v2.0 - Loneliness
1863	NIH Toolbox - Bank FF v2.0 - Friendship
1863	NIH Toolbox - Bank Fixed Form v2.0 - Friendship
1864	NIH Toolbox - Bank v2.0 - Friendship
1864	NIH Toolbox - Bank v2.0 - Friendship
1865	PROMIS Item Bank v1.0 – Substance Use/Alcohol: Alcohol Use
1865	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Substance Use/Alcohol: Alcohol Use
1866	WPAI+CIQ:AS
1866	Work Productivity and Activity Impairment Questionnaire plus Classroom Impairment Questions: Allergy Specific
1867	FACT-En
1867	Functional Assessment of Cancer Therapy - Endometrial
1868	PROMIS Item Bank v1.0 – Emotional Distress - Anxiety
1868	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Emotional Distress - Anxiety
1869	RS
1869	Resilience Scale
1870	PROMIS Item Bank v1.0 – Severity of Substance Use – Past 3 months
1870	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Severity of Substance Use – Past 3 months
1871	PROMIS Item Bank v1.0 – Severity of Substance Use – Past 30 days
1871	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Severity of Substance Use – Past 30 days
1872	PROMIS Item Bank v1.0 – Appeal of Substance Use - Past 30 days
1872	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Appeal of Substance Use - Past 30 days
1873	PROMIS Item Bank v1.0 – Smoking: Negative Health Expectancies for Daily Smokers
1873	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Negative Health Expectancies for Daily Smokers
1874	PROMIS Item Bank v1.0 – Smoking: Negative Health Expectancies for Nondaily Smokers

1874	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Negative Health Expectancies for Nondaily Smokers
1875	PROMIS Item Bank v1.0 – Smoking: Negative Health Expectancies for All Smokers
1875	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Negative Health Expectancies for All Smokers
1876	PROMIS Item Bank v1.0 – Smoking: Nicotine Dependence for All Smokers
1876	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Nicotine Dependence for All Smokers
1877	WPAI:AA
1877	Work Productivity and Activity Impairment Questionnaire: Allergic Asthma, Version 2
1878	WPAI:MS v2.0
1878	Work Productivity and Activity Impairment Questionnaire: Multiple Sclerosis, Version 2.0
1879	WPAI: Constipation v2.0
1879	Work Productivity and Activity Impairment Questionnaire: Constipation, Version 2.0
1880	WPAI:CU v2.0
1880	Work Productivity and Activity Impairment Questionnaire: Chronic Urticaria, Version 2.0
1881	WPAI:CRPC v2.0
1881	Work Productivity and Activity Impairment Questionnaire: Castration-Resistant Prostate Cancer, Version 2.0
1882	WPAI+CIQ:IBS v2.0
1882	Work Productivity and Activity Impairment Questionnaire: plus Classroom Impairment Questionnaire, Irritable Bowel Syndrome, Version 2.0
1883	WPAI:DU v2.0
1883	Work Productivity and Activity Impairment Questionnaire: Digital Ulcers, Version 2.0
1884	WPAI:UF v2.0
1884	Work Productivity and Activity Impairment Questionnaire: Uterine Fibroids, Version 2.0
1885	PROMIS SexFS Bank v1.0 - Interest in Sexual Activity
1885	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v1.0 – Interest in Sexual Activity
1886	PROMIS SexFS Pool v1.0 - Sexual Function Screener
1886	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v1.0 – Sexual Function Screener
1887	PROMIS SexFS Pool v1.0 - Therapeutic Aids
1887	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v1.0 – Therapeutic Aids

1888	CUDOS
1888	Clinically Useful Depression Outcome Scale
1889	OCDUS
1889	Obsessive Compulsive Drug Use Scale
1890	DDQ
1890	Desire for Drug Questionnaire
1891	SEMCD-S
1891	Self-Efficacy for Managing Chronic Disease - Spanish version
1892	HIVTSQc
1892	HIV Treatment Satisfaction Questionnaire - Change version
1893	KSQ
1893	King's Sarcoidosis Questionnaire
1894	PROMIS Ca Item Bank v1.0 - Emotional Distress - Anxiety
1894	Patient-Reported Outcomes Measurement Information System Ca Item Bank v1.0 - Emotional Distress - Anxiety
1895	NIH Toolbox - Parent Report Bank FF v2.0 - Positive Peer Interaction
1895	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Positive Peer Interaction
1896	NIH Toolbox - Parent Report Bank FF v2.0 - Peer Rejection
1896	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Peer Rejection
1897	NIH Toolbox Parent Report Bank v2.0 - Positive Peer Interaction
1897	NIH Toolbox Parent Report Bank v2.0 - Positive Peer Interaction
1898	NIH Toolbox - Parent Report Bank v2.0 - Social Withdrawal
1898	NIH Toolbox - Parent Report Bank v2.0 - Social Withdrawal
1899	NIH Toolbox - Parent Report Bank v2.0 - Peer Rejection
1899	NIH Toolbox - Parent Report Bank v2.0 - Peer Rejection
1900	NIH Toolbox - Bank FF B v2.0 - General Life Satisfaction
1900	NIH Toolbox - Bank Fixed Form B v2.0 - General Life Satisfaction
1901	NIH Toolbox - Bank FF A v2.0 - General Life Satisfaction
1901	NIH Toolbox - Bank Fixed Form A v2.0 - General Life Satisfaction
1902	NIH Toolbox - Bank FF v2.0 - Anger - Affect
1902	NIH Toolbox - Bank Fixed Form v2.0 - Anger - Affect
1903	NIH Toolbox - Bank v2.0 - Self-Efficacy

1903	NIH Toolbox - Bank v2.0 - Self-Efficacy
1904	NIH Toolbox - Domain-Specific Life Satisfaction Survey
1904	NIH Toolbox - Domain-Specific Life Satisfaction Survey
1905	NIH Toolbox - Maternal Relationship Survey
1905	NIH Toolbox - Maternal Relationship Survey
1906	NIH Toolbox - Emotion Control Survey
1906	NIH Toolbox - Emotion Control Survey
1907	NIH Toolbox - Apathy Survey
1907	NIH Toolbox - Apathy Survey
1908	PSS10
1908	Perceived Stress Scale 10 items
1909	WPAI:Melanoma
1909	Work Productivity and Activity Impairment Questionnaire: Melanoma
1910	WPAI:Nocturia
1910	Work Productivity and Activity Impairment Questionnaire: Nocturia
1911	PSS4
1911	Perceived Stress Scale 4 items
1912	PROMIS Item Bank v1.0 – Smoking: Negative Psychosocial Expectancies for Daily Smokers
1912	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Negative Psychosocial Expectancies for Daily Smokers
1913	PROMIS Item Bank v1.0 – Smoking: Nicotine Dependence for Nondaily Smokers
1913	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Nicotine Dependence for Nondaily Smokers
1914	PROMIS Item Bank v1.0 – Smoking: Nicotine Dependence for Daily Smokers
1914	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Nicotine Dependence for Daily Smokers
1915	QSU-Brief
1915	Brief Questionnaire on Smoking Urge
1916	PROMIS Item Bank v1.0 Substance Use/Alcohol: Positive Expectancies
1916	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 Substance Use/Alcohol: Positive Expectancies
1917	PROMIS Ca Item Bank v1.0 - Emotional Distress - Depression
1917	Patient-Reported Outcomes Measurement Information System Ca Item Bank v1.0 - Emotional Distress - Depression

1918	WPAI:AA-IVRS
1918	Work Productivity and Activity Impairment Questionnaire: Allergic Asthma, Interactive Voice Response System
1919	WPAI:FMS-Pain
1919	Work Productivity and Activity Impairment Questionnaire: Pain Associated with Fibromyalgia, Version 2.0
1920	WPAI:NV v2.0
1920	Work Productivity and Activity Impairment Questionnaire: Nausea and Vomiting, Version 2.0
1921	WPAI:PsA v2.0
1921	Work Productivity and Activity Impairment Questionnaire: Psoriatic Arthritis, Version 2.0
1922	WPAI:US v2.0
1922	Work Productivity and Activity Impairment Questionnaire: Urinary Symptoms, Version 2.0
1923	WPAI:TTR Amyloidosis v2.0
1923	Work Productivity and Activity Impairment Questionnaire: TTR Amyloidosis, Version 2.0
1924	WPAI:Headache v2.0
1924	Work Productivity and Activity Impairment Questionnaire: Headache, Version 2.0
1925	WPAI:COPD v2.0
1925	Work Productivity and Activity Impairment Questionnaire: Chronic Obstructive Pulmonary Disease, Version 2.0
1926	PROMIS SexFS Bank v1.0 - Lubrication
1926	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v1.0 – Lubrication
1927	PROMIS SexFS Bank v1.0 - Orgasm
1927	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v1.0 – Orgasm
1928	PROMIS SexFS Pool v1.0 - Sexual Activities
1928	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v1.0 – Sexual Activities
1929	CPSI
1929	Chronic Pain Sleep Inventory
1930	ALS Survey
1930	Amyotrophic Lateral Sclerosis Survey
1931	HIVTSQs
1931	HIV Treatment Satisfaction Questionnaire - Status version

1932	NIH Toolbox - Parent Report Bank v2.0 - Fear - Over Anxious
1932	NIH Toolbox - Parent Report Bank v2.0 - Fear - Over Anxious
1933	NIH Toolbox - Parent Report Bank FF v2.0 - Fear - Over Anxious
1933	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Fear - Over Anxious
1934	NIH Toolbox - Parent Report Bank FF v2.0 - Empathic Behaviors
1934	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Empathic Behaviors
1935	NIH Toolbox - Parent Report Bank v2.0 - Empathic Behaviors
1935	NIH Toolbox - Parent Report Bank v2.0 - Empathic Behaviors
1936	NIH Toolbox - Bank FF v2.0 - Positive Affect
1936	NIH Toolbox - Bank Fixed Form v2.0 - Positive Affect
1937	NIH Toolbox - Bank v2.0 - General Life Satisfaction
1937	NIH Toolbox - Bank v2.0 - General Life Satisfaction
1938	NIH Toolbox - Bank v2.0 - Positive Affect
1938	NIH Toolbox - Bank v2.0 - Positive Affect
1939	NIH Toolbox - Bank FF v2.0 - Perceived Stress
1939	NIH Toolbox - Bank Fixed Form v2.0 - Perceived Stress
1940	NIH Toolbox - Bank v2.0 - Perceived Stress
1940	NIH Toolbox - Bank v2.0 - Perceived Stress
1941	NIH Toolbox - Bank FF v2.0 - Self Efficacy
1941	NIH Toolbox - Bank Fixed Form v2.0 - Self Efficacy
1942	NIH Toolbox - Bank v2.0 - Sadness
1942	NIH Toolbox - Bank v2.0 - Sadness
1943	WPAI:IBS-C
1943	Work Productivity and Activity Impairment: Irritable Bowel Syndrome with Constipation
1944	NIH Toolbox - Parent report - Domain-Specific Life Satisfaction Survey
1944	NIH Toolbox - Parent report - Domain-Specific Life Satisfaction Survey
1945	NIH Toolbox - Paternal Relationship Survey
1945	NIH Toolbox - Paternal Relationship Survey
1946	PROMIS Item Bank v1.0 – Appeal of Substance Use - Past 3 months
1946	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Appeal of Substance Use - Past 3 months
1947	PROMIS Item Bank v1.0 – Smoking: Coping Expectancies for All Smokers

1947	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Coping Expectancies for All Smokers
1948	PROMIS Item Bank v1.0 – Smoking: Coping Expectancies for Daily Smokers
1948	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Smoking: Coping Expectancies for Daily Smokers
1949	RS10
1949	Resilience Scale for Children
1950	WPAI:BD
1950	Work Productivity and Activity Impairment Questionnaire: Bipolar Disorder
1951	NSS
1951	Narcolepsy Severity Scale
1952	WPAI:Spondyloarthritis v2.0
1952	Work Productivity and Activity Impairment Questionnaire: Spondyloarthritis, Version 2.0
1953	WPAI:TTR Amyloidosis-CG v2.0
1953	Work Productivity and Activity Impairment Questionnaire: TTR Amyloidosis-Caregiver, Version 2.0
1954	PROMIS SexFS Bank v1.0 - Global Satisfaction with Sex Life
1954	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v1.0 – Global Satisfaction with Sex Life
1955	PROMIS SexFS Pool v1.0 - Anal Discomfort
1955	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v1.0 – Anal Discomfort
1956	EAR-Q
1956	EAR-Questionnaire
1957	SEMCD
1957	Self-Efficacy for Managing Chronic Disease
1958	NIH Toolbox - Sensation and Pain - Pain Interference Survey
1958	NIH Toolbox - Sensation and Pain - Pain Interference Survey
1959	NIH Toolbox - Sensation and Pain - Pain Intensity Survey
1959	NIH Toolbox - Sensation and Pain - Pain Intensity Survey
1960	NIH Toolbox - Sensation and Pain - Vision-Related Quality of Life Survey
1960	NIH Toolbox - Sensation and Pain - Vision-Related Quality of Life Survey
1961	IEQ
1961	IEQ-EU

1961	Involvement Evaluation Questionnaire
1962	NIH Toolbox - Parent Report Bank FF v2.0 - Fear- Separation Anxiety
1962	NIH Toolbox - Parent Report Bank Fixed Form v2.0 - Fear- Separation Anxiety
1963	NIH Toolbox - Parent Report Bank v2.0 - Fear- Separation Anxiety
1963	NIH Toolbox - Parent Report Bank v2.0 - Fear- Separation Anxiety
1964	NIH Toolbox - Bank v2.0 - Emotional Support
1964	NIH Toolbox - Bank v2.0 - Emotional Support
1965	NIH Toolbox - Bank FF v2.0 - Emotional Support
1965	NIH Toolbox - Bank Fixed Form v2.0 - Emotional Support
1966	NIH Toolbox - Bank FF v2.0 - Anger
1966	NIH Toolbox - Bank Fixed Form v2.0 - Anger
1967	NIH Toolbox - Bank v2.0 - Anger
1967	NIH Toolbox - Bank v2.0 - Anger
1968	NIH Toolbox - Bank FF v2.0 - Anger - Physical Aggression
1968	NIH Toolbox - Bank Fixed Form v2.0 - Anger - Physical Aggression
1969	NIH Toolbox - Bank FF v2.0 - Anger - Hostility
1969	NIH Toolbox - Bank Fixed Form v2.0 - Anger - Hostility
1970	NIH Toolbox - Bank v2.0 - Anger - Physical Aggression
1970	NIH Toolbox - Bank v2.0 - Anger - Physical Aggression
1971	NIH Toolbox - Bank v2.0 - Anger - Affect
1971	NIH Toolbox - Bank v2.0 - Anger - Affect
1972	NIH Toolbox - Positive Parent Relationship Survey
1972	NIH Toolbox - Positive Parent Relationship Survey
1973	RS14
1973	Resilience Scale 14-items
1974	WPAI:PSO
1974	Work Productivity and Activity Impairment Questionnaire: Psoriasis
1975	PROMIS Item Bank v1.0 Substance Use/Alcohol: Negative Expectancies
1975	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 Substance Use/Alcohol: Negative Expectancies
1976	PROMIS Item Bank v1.0 – Substance Use/Alcohol: Negative Consequences

1976	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 – Substance Use/Alcohol: Negative Consequences
1977	PROMIS Item Bank v1.0 Substance Use/Alcohol: Positive Consequences
1977	Patient-Reported Outcomes Measurement Information System Item Bank v1.0 Substance Use/Alcohol: Positive Consequences
1978	FKSI-15
1978	Functional Assessment of Cancer Therapy-Kidney Symptom Index
1979	WPAI:IBD
1979	Work Productivity and Activity Impairment Questionnaire: Inflammatory Bowel Disease, Version 2.0
1980	PROMIS SexFS Profile v1.0 – Female
1980	PROMIS Sexual Function and Satisfaction Profile v1.0 – Female
1981	PROMIS SexFS Profile v1.0 – Male
1981	PROMIS Sexual Function and Satisfaction Profile v1.0 – Male
1982	WPAI:RS v2.0
1982	Work Productivity and Activity Impairment Questionnaire: Respiratory Symptoms, Version 2.0
1983	WPAI:Hidradenitis Suppurativa v2.0
1983	Work Productivity and Activity Impairment Questionnaire: Hidradenitis Suppurativa Version 2.0
1984	PROMIS SexFS Profile v1.0 – Male & Female
1984	PROMIS Sexual Function and Satisfaction Profile v1.0 – Male & Female
1985	WPAI:CRPC-CG v2.0
1985	Work Productivity and Activity Impairment Questionnaire: Castration-Resistant Prostate Cancer Caregiver, Version 2.0
1986	PROMIS SexFS Bank v1.0 - Erectile Function
1986	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v1.0 – Erectile Function
1987	WPAI:MPS-VII-Caregiver v2.0
1987	Work Productivity and Activity Impairment Questionnaire: Mucopolysaccharidosis type VII, Version 2.0
1988	PROMIS SexFS Bank v1.0 - Vaginal Discomfort
1988	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Bank v1.0 – Vaginal Discomfort
1989	PROMIS SexFS Pool v1.0 - Interfering Factors
1989	Patient-Reported Outcomes Measurement Information System Sexual Function and Satisfaction Pool v1.0 – Interfering Factors

1990	ETISR-SF
1990	Early Trauma Inventory Self Report - Short Form
1991	DRRI
1991	Deployment Risk and Resilience Inventory
1992	A-FICSI
1992	Adolescent Fecal Incontinence and Constipation Symptom Index
1993	FIC QOL
1993	Fecal Incontinence and Constipation Quality of Life
1994	FSSG
1994	Frequency Scale for the Symptoms of GERD
1995	KDQOL-SF
1995	Kidney Disease Quality of Life instrument - Short form
1996	MPN-SAF
1996	MyeloProliferative Neoplasm Symptom Assessment Form
1997	BENS Score
1997	Bowel Endometriosis Syndrome Score
1998	WPAI:HC v2
1998	Work Productivity and Activity Impairment Questionnaire: Heart Condition, Version 2
1999	WPAI:UC-CG
1999	Work Productivity and Activity Impairment Questionnaire: Ulcerative Colitis, for child's caregiver, Version 2
2000	SUPPH-29
2000	Strategies Used by People to Promote Health
2001	PADL-ALS
2001	Patient Activity of Daily Living scale for patients with Amyotrophic Lateral Sclerosis
2002	DSI
2002	Disability Severity Index
2003	nOH-ADL
2003	Neurogenic Orthostatic Hypotension Activities of Daily Living
2004	EQ-5D-5L
2004	EuroQoL 5-Dimension 5-Level
2005	ICIQ-N

2005	International Consultation on Incontinence Questionnaire Nocturia Module
2006	ICIQ-UAB
2006	International Consultation on Incontinence Questionnaire Under Active Bladder
2007	CUXOS-D
2007	Clinically Useful Anxiety Outcome Scale - Daily version
2008	ASCQ-Me - Cognitive Impact
2008	Adult Sickle Cell Quality of Life Measurement Information System - Cognitive Impact
2009	ASCQ-Me - Emotional Impact
2009	Adult Sickle Cell Quality of Life Measurement Information System - Emotional Impact
2010	ASCQ-Me - Pain
2010	Adult Sickle Cell Quality of Life Measurement Information System - Pain
2011	BYI-2
2011	Beck Youth Inventories - Second Edition
2012	CCBS
2012	Child's Challenging Behaviour Scale
2013	WPAI+CIQ:HS
2013	Work Productivity and Activity Impairment Questionnaire plus Classroom Impairment Questionnaire: Hemophilia Specific
2014	advSM-SAF
2014	Advanced Systemic Mastocytosis Symptom Assessment Form
2015	CES
2015	Combat Exposure Scale
2016	WPAI:DD
2016	Work Productivity and Activity Impairment Questionnaire: Daily Drowsiness, Version 2
2017	WPAI:SMA-CG
2017	Work Productivity and Activity Impairment Questionnaire: Spinal Muscular Atrophy, for Caregivers, Version 2
2018	HS-FOCUS Patient version
2018	Hunter Syndrome-Functional Outcomes for Clinical Understanding Scale - Patient version
2019	QLQ-AA/PNH
2019	Quality of Life Questionnaire for patients with Aplastic Anemia and/or Paroxysmal Nocturnal Hemoglobinuria
2020	DRRI-2 - Unit Social Support

2020	Deployment Risk & Resilience Inventory-2 - Unit Social Support
2021	DRRI-2 - General Harassment
2021	Deployment Risk & Resilience Inventory-2 - General Harassment
2022	DRRI-2 - Sexual Harassment
2022	Deployment Risk & Resilience Inventory-2 - Sexual Harassment
2023	ICIQ-VS
2023	International Consultation on Incontinence Questionnaire Vaginal Symptoms Module
2024	CUSADOS
2024	Clinically Useful Social Anxiety Disorder Outcome Scale
2025	CHRT-SR12
2025	Concise Health Risk Tracking Self-Report scale - 12 item self-report
2026	ASCQ-Me SF - Stiffness Impact
2026	Adult Sickle Cell Quality of Life Measurement Information System Short Form - Stiffness Impact
2027	C-CAP2
2027	Cardiff Cardiac Ablation PROM - Post-ablation
2028	WPAI:Migraine
2028	Work Productivity and Activity Impairment Questionnaire: Migraine
2029	Patient Reported Outcomes, Burdens and Experiences
2030	SAQ
2030	Severe Asthma Questionnaire
2031	WPAI:Hypoparathyroidism
2031	Work Productivity and Activity Impairment Questionnaire: Hypoparathyroidism, Version 2
2032	TOS
2032	Treatment Outcome Score
2033	MSCS
2033	Mean Symptom Complex Severity score
2034	GIDYQ-AA
2034	Gender Identity/Gender DYsphoria Questionnaire for Adolescents and Adults
2035	MPSAS
2035	Mesenteric Panniculitis Subjective Assessment Score
2036	QoL-PCD

2036	Quality of Life instrument for Primary Ciliary Dyskinesia
2037	DRRI-2 - Deployment Support from Family and Friends
2037	Deployment Risk & Resilience Inventory-2 - Deployment Support from Family and Friends
2038	DRRI-2 - Preparedness
2038	Deployment Risk & Resilience Inventory-2 - Preparedness
2039	mJOA
2039	modified Japanese Orthopaedic Association scale
2040	ICIQ-B
2040	International Consultation on Incontinence Questionnaire Anal Incontinence Symptoms and Quality of Life Module
2041	RLS-6
2041	Restless Legs Syndrome - 6 Rating Scales
2042	QOLIBRI-OS
2042	Quality of Life after Brain Injury - Overall Scale
2043	ASCQ-Me - Social Functioning Impact
2043	Adult Sickle Cell Quality of Life Measurement Information System - Social Functioning Impact
2044	ASCQ-Me - Sleep Impact
2044	Adult Sickle Cell Quality of Life Measurement Information System - Sleep Impact
2045	OPQOL-Brief
2045	Older People’s Quality of Life - Brief version
2046	WPAI+CIQ:Asthma
2046	Work Productivity and Activity Impairment Questionnaire plus Classroom Impairment Questionnaire: Asthma
2047	emPHasis-10
2047	emPHasis-10
2048	WPAI:D
2048	Work Productivity and Activity Impairment Questionnaire: Depression, Version 2
2049	WPAI:Hypoparathyroidism, Interviewer Version
2049	Work Productivity and Activity Impairment Questionnaire: Hypoparathyroidism, Interviewer Version, Version 2
2050	WPAI:CC
2050	Work Productivity and Activity Impairment Questionnaire: Chronic Constipation, Version 2
2051	DRRI-2 - Family Stressors

2051	Deployment Risk & Resilience Inventory-2 - Family Stressors
2052	DRRI-2 - Concerns about Life and Family Disruptions
2052	Deployment Risk & Resilience Inventory-2 - Concerns about Life and Family Disruptions
2053	DRRI-2 - Postdeployment Stressors
2053	Deployment Risk & Resilience Inventory-2 - Postdeployment Stressors
2054	ARMLQ
2054	Age-Related Muscle Loss Questionnaire
2055	SarQoL
2055	Sarcopenia-specific Quality of Life questionnaire
2056	CUXOS
2056	Clinically Useful anXiety Outcome Scale
2057	ICIQ-Nqol
2057	International Consultation on Incontinence Questionnaire Nocturia Quality of Life Module
2058	ICIQ-OABqol
2058	International Consultation on Incontinence Questionnaire Overactive Bladder Quality of Life Module
2059	DSMQ-R
2059	Diabetes Self-Management Questionnaire - Revised
2060	Brief COPE
2060	Brief COPE
2061	ASCQ-Me SF - Social Functioning Impact
2061	Adult Sickle Cell Quality of Life Measurement Information System Short Form - Social Functioning Impact
2062	ASCQ-Me SF - Pain Episodes
2062	Adult Sickle Cell Quality of Life Measurement Information System Short Form - Pain Episodes
2063	ASCQ-Me SF - Sleep Impact
2063	Adult Sickle Cell Quality of Life Measurement Information System Short Form - Sleep Impact
2064	ASCQ-Me SF - Pain Impact
2064	Adult Sickle Cell Quality of Life Measurement Information System Short Form - Pain Impact
2065	KDQOL-36 Survey
2065	Kidney Disease Quality of Life instrument - 36 items
2066	ICIQ-Bladder Diary

2066	International Consultation on Incontinence Questionnaire Bladder Diary
2067	ICIQ-CLUTS
2067	International Consultation on Incontinence Questionnaire Paediatric Lower Urinary Tract Symptoms
2068	ICIQ-PadPROM
2068	International Consultation on Incontinence Questionnaire Absorbent Pads
2069	PAM-D21
2069	Perceptions About Medications for Diabetes - 21 items
2070	ICIQ-FLUTS LF
2070	International Consultation on Incontinence Questionnaire-Female Lower Urinary Tract Symptoms - Long Form
2071	ESDS
2071	Enforced Social Dependency scale
2072	WPAI:Muscle
2072	Work Productivity and Activity Impairment Questionnaire: Muscle disease 2.0
2073	WPAI:FMS
2073	Work Productivity and Activity Impairment Questionnaire: Fibromyalgia symptoms, Version 2
2074	HAL
2074	Hemophilia Activities List
2075	WPAI:OA-Knee or Hip
2075	Work Productivity and Activity Impairment Questionnaire: Osteoarthritis of the knee or hip, Version 2
2076	QOLIBRI
2076	Quality of Life after Brain Injury
2077	PESaM
2077	Patient Experiences and Satisfaction with Medications
2078	DRRI-2 - Combat Experiences
2078	Deployment Risk & Resilience Inventory-2 - Combat Experiences
2079	DRRI-2 - Difficult Living and Working Environment
2079	Deployment Risk & Resilience Inventory-2 - Difficult Living and Working Environment
2080	DRRI-2 - Childhood Family Functioning
2080	Deployment Risk & Resilience Inventory-2 - Childhood Family Functioning
2081	DRRI-2 - Prior Stressors

2081	Deployment Risk & Resilience Inventory-2 - Prior Stressors
2082	DRRI-2 - Postdeployment Social Support
2082	Deployment Risk & Resilience Inventory-2 - Postdeployment Social Support
2083	DRRI-2 - Postdeployment Family Functioning
2083	Deployment Risk & Resilience Inventory-2 - Postdeployment Family Functioning
2084	UCLA SCTC GIT
2084	University of California, Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument
2085	ADCT
2085	Atopic Dermatitis Control Tool
2086	ICIQ-LTCqol
2086	International Consultation on Incontinence Long-Term Indwelling Catheter Users
2087	ASCQ-Me SF - Emotional Impact
2087	Adult Sickle Cell Quality of Life Measurement Information System Short Form - Emotional Impact
2088	ASCQ-Me - Stiffness Impact
2088	Adult Sickle Cell Quality of Life Measurement Information System - Stiffness Impact
2089	WPAI:DNP
2089	Work Productivity and Activity Impairment Questionnaire: Leg and Foot Pain
2090	PedHAL
2090	Paediatric Haemophilia Activities List
2091	WPAI:OA-Knee
2091	Work Productivity and Activity Impairment Questionnaire: Osteoarthritis of the knee, Version 2
2092	RGEI
2092	Revised Grief Experience Inventory
2093	CUDOS-A
2093	Clinically Useful Depression Outcome Scale supplemented with questions for the DSM-5 anxious distress specifier
2094	CUDOS-D
2094	Clinically Useful Depression Outcome Scale - Daily version
2095	GPSQ
2095	Gender Preoccupation and Stability Questionnaire
2096	UGDS-F

2096	Utrecht Gender Dysphoria Scale - Female version
2097	Shortened HS-FOCUS - Patient version
2097	Hunter Syndrome-Functional Outcomes for Clinical Understanding Scale - Shortened version - Patient version
2098	ITP-PAQ
2098	Immune Thrombocytopenic Purpura Patient Assessment Questionnaire
2099	ITP-QoL
2099	Quality of Life questionnaire for children & adolescents with Idiopathic Thrombocytopenic Purpura
2100	DRRI-2 - Perceived Threat
2100	Deployment Risk & Resilience Inventory-2 - Perceived Threat
2101	DRRI-2 - Aftermath of Battle
2101	Deployment Risk & Resilience Inventory-2 - Aftermath of Battle
2102	DRRI-2 - NBC Exposures
2102	Deployment Risk & Resilience Inventory-2 - NBC Exposures
2103	ICIQ-OAB
2103	International Consultation on Incontinence Questionnaire Overactive Bladder Module
2104	ICIQ-IBD
2104	International Consultation on Incontinence Questionnaire Inflammatory Bowel Disease
2105	CH-RLSq13
2105	Cambridge - Hopkins Restless Legs Syndrome Short Form 2 DIAGNOSTIC QUESTIONNAIRE
2106	NSC
2106	Nurse Stress Checklist
2107	SCD-MHC
2107	Sickle Cell Disease Medical History Checklist
2108	IBS-QOL
2108	Irritable Bowel Syndrome - Quality Of Life
2109	I-PSS
2109	International Prostate Symptom Score
2110	IWLS
2110	Impact of Weight Loss Scale
2111	KAP

2111	Kingsley Alopecia Profile
2112	KDQOL
2112	Kidney Disease Quality of Life instrument
2113	MAC
2113	Mental Adjustment to Cancer Scale
2114	MFSQ
2114	McCoy Female Sexuality Questionnaire
2115	PMSES
2115	Broome Pelvic Muscle Exercise Self-Efficacy Scale
2116	POMS
2116	Profile of Mood States
2117	POS
2117	Palliative Care Outcome Scale
2118	PROSQOLI
2118	Prostate Cancer Specific Quality of Life Instrument
2119	QLQ or CEQ
2119	Quality of Life Questionnaire or Client Experiences Questionnaire
2120	QLQ-Asthma
2120	Questionnaire for the Assessment of Quality of Life in Asthma Patients
2121	PIADS
2121	Psychosocial Impact of Assistive Device Scale
2122	PLC
2122	Quality of Life Profile for the Chronically Ill
2123	PQoL
2123	Perceived Quality of Life scale
2124	PHQ
2124	Patient Health Questionnaire
2125	PRQLQ
2125	Paediatric Rhinoconjunctivitis Quality of Life Questionnaire
2126	PACQLQ
2126	Paediatric Asthma Caregiver's Quality of Life Questionnaire

2127	PAQ
2127	Peripheral Artery Questionnaire
2128	Q-LES-Q
2128	Quality of Life Enjoyment and Satisfaction Questionnaire
2129	QLQ
2129	Quality of Life Questionnaire
2130	QL-SP
2130	Quality of Life Questionnaire for Cardiac Spouses
2131	QLS-BC
2131	Quality of Life Schedule
2132	QOL-CA
2132	Quality of Life Cancer Scale
2133	PSMS
2133	Physical Self-Maintenance Scale
2134	QL
2134	Quality of Life
2135	QLI-CP
2135	Quality of Life Index for Colostomy Patients
2136	MRF26
2136	Maugeri Foundation Respiratory Failure Questionnaire
2137	MSQOL-54
2137	Multiple Sclerosis Quality of Life-54
2138	PAID
2138	Problem Areas in Diabetes scale
2139	PDI
2139	Psoriasis Disability Index
2140	PFSDQ-M
2140	Pulmonary Functional Status & Dyspnea Questionnaire-Modified
2141	SKINFECT PRO
2141	Acute Bacterial Skin and Skin Structure Infections Symptom Diary
2142	MSWDQ

2142	Multiple Sclerosis Work Difficulties Questionnaire
2143	FACT-GOG-NTX
2143	Functional Assessment of Cancer Therapy - Gynecologic Oncology Group-Neurotoxicity
2144	CHRT-SR14
2144	CHRT-SR14 - Concise Health Risk Tracking - 14-item self-report
2145	NAVQ
2145	Near Activity Visual Questionnaire
2146	PRISM
2146	Patient-Reported Impact of Scars Measure
2147	QoL-AGHDA
2147	Quality of Life Assessment of Growth Hormone Deficiency in Adults
2148	FDM
2148	Family Disruption Measure-Chickenpox
2149	PRIMUS
2149	Patient Reported Outcome indices for Multiple Sclerosis
2150	LCOPD
2150	Living with Chronic Obstructive Pulmonary Disease
2151	PD Home Diary
2151	Parkinson's Disease Home Diary
2152	FACIT-Pal
2152	Functional Assessment of Chronic Illness Therapy - Palliative Care
2153	FACIT-AD
2153	Functional Assessment of Chronic Illness Therapy for Patients With Abdominal symptoms
2154	UAS7
2154	Urticaria Activity Score
2155	UAS
2155	Urticaria Activity Score
2156	PSAAD
2156	Pruritus and Symptoms Assessment for Atopic Dermatitis
2157	ItchApp
2157	ItchApp

2158	PKU-POMS
2158	Profile of Mood States - Phenylketonuria
2159	AS-WIS
2159	Ankylosing Spondylitis Work Instability Scale
2160	MS-WIS
2160	Multiple Sclerosis - specific Work Instability Scale
2161	NFI-MND
2161	Neurological Fatigue Index - Motor Neurone Disease
2162	NFI-MS
2162	Neurological Fatigue Index - Multiple Sclerosis
2163	LSS
2163	Leeds Spasticity Scale
2164	TBI-WIS
2164	Traumatic Brain Injury Work Instability Scale
2165	PBI-Vit
2165	Patient Benefit Index - Vitiligo
2166	USE-MS
2166	Unidimensional Self Efficacy Scale for Multiple Sclerosis
2167	PneumoPRO
2167	Community-Acquired Bacterial Pneumonia Symptom Diary
2168	P-OMAQ-P
2168	Pediatric Oral Medicine Acceptability Questionnaire - Patient Version
2169	Adapted INHIB-QoL
2169	Inhibitor-Specific Quality of Life with Aspects of Caregiver Burden
2170	FACT-EGFRI-18
2170	Functional Assessment of Cancer Therapy - Epidermal Growth Factor Receptor Inhibitors
2171	ThyTSQ
2171	Underactive Thyroid Treatment Satisfaction Questionnaire
2172	ABOUT—Dependence
2172	ABOUT—Dependence
2173	OnyCOE-t

2173	Quality of Life Questionnaire Onychomycosis (Nail fungal condition)
2174	PSORIQoL
2174	Psoriasis Index of Quality of Life
2175	PlexiQoL
2175	Plexiform neurofibromas Quality of Life measure
2176	PNIQ
2176	Parenteral Nutrition Impact Questionnaire
2177	CLIQ
2177	Crohn's Life Impact Questionnaire
2178	OAQoL
2178	Osteoarthritis Quality of Life measure
2179	DDS
2179	Diabetes Distress Scale
2180	DDS2
2180	Brief Diabetes Distress Screening Instrument
2181	FACT-BMT
2181	Functional Assessment of Cancer Therapy - Bone Marrow Transplantation
2182	FACIT-AI
2182	Functional Assessment of Chronic Illness Therapy-Ascites Index
2183	FACT-Cog
2183	Functional Assessment of Cancer Therapy - Cognitive function issues
2184	FoRSe
2184	Fear of Recurrence Scale
2185	ADerm-SS
2185	Atopic Dermatitis Symptom Scale
2186	ADerm-IS
2186	Atopic Dermatitis Impact Scale
2187	BD-QoL
2187	Behçet's disease Quality of Life
2188	HypoA-Q SF
2188	Hypoglycaemia Awareness Questionnaire Short Form

2189	VLU-QoL
2189	Venous Leg Ulcer Quality of Life
2190	ENAT
2190	Arthritis Educational Needs Assessment Tool
2191	NSI-MS
2191	Neurological Sleep Index - Multiple Sclerosis
2192	Nurse-WIS
2192	Nurse-Work Instability Scale
2193	FBlSI
2193	Functional Assessment of Cancer Therapy - Bladder Symptom Index
2194	NFHNSI-22
2194	National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy - Head & Neck Symptom Index
2195	OAB-q SF (4-week recall)
2195	OverActive Bladder questionnaire - Short-form (4-week recall)
2196	OAB-V3
2196	OverActive Bladder Awareness Tool - 3-item
2197	RDQ
2197	Remission for Depression Questionnaire
2198	IHSS
2198	Idiopathic Hypersomnia Severity Scale
2199	FPSI-7
2199	Functional Assessment of Cancer Therapy - Prostate Symptom Index
2200	FACIT-TS-BTCSQ
2200	Functional Assessment of Chronic Illness Therapy - Bone Treatment Convenience and Satisfaction Questionnaire
2201	DSAS-1
2201	Type 1 Diabetes Stigma Assessment Scale
2202	MSWDQ-23
2202	Multiple Sclerosis Work Difficulties Questionnaire - Short version
2203	FACT-EF
2203	Functional Assessment of Cancer Therapy - Enteral Feeding

2204	FACIT-TS-G
2204	Functional Assessment of Chronic Illness Therapy - Treatment Satisfaction - General
2205	faVIQ
2205	Functional ability Quality of Vision
2206	APPLIQue
2206	Alzheimer's Patient Partners Life Impact Questionnaire
2207	BOCLIR
2207	Bowel Cleansing Impact Review
2208	ALIS
2208	Asthma Life Impact Scale
2209	WISP
2209	Well-Being in Surgical Patients
2210	UGAQoL
2210	Urogenital Atrophy Quality of Life
2211	IQoLI
2211	Incontinence Quality of Life Index
2212	FACIT-CD
2212	Functional Assessment of Chronic Illness Therapy - Cervical Dysplasia
2213	FACT-BP
2213	Functional Assessment of Cancer Therapy - Bone Pain
2214	CDI-DaySyms
2214	Clostridium Difficile Infection Daily Symptoms
2215	SCI-CAT
2215	Spinal Cord Injury Computer Adaptive Test
2216	ItchyQoL - Frequency version
2216	ItchyQoL - Frequency version
2217	PBI-P
2217	Patient Benefit Index- Pruritus
2218	PAHQoL
2218	Pulmonary Arterial Hypertension Quality of Life
2219	HypoA-Q Past month

2219	Hypoglycaemia Awareness Questionnaire Past month
2220	LFIS-RA
2220	Leeds Foot Impact Scale for Rheumatoir Arthristis
2221	LMSQOL
2221	Leeds Multiple Sclerosis Quality of Life scale
2222	NFI-Stroke
2222	Neurological Fatigue Index - Stroke
2223	SSc-QoL
2223	Systemic Sclerosis Quality of Life Scale
2224	Stroke-QoL
2224	Systemic Sclerosis Quality of Life Scale
2225	PBI 2.0
2225	Patient Benefit Index 2.0
2226	PBI-AS
2226	Patient Benefit Index - Aged skin
2227	PBI-HE
2227	Patient Benefit Index - Chronic Hand Eczema
2228	OAB-V8
2228	OverActive Bladder Awareness Tool - 8-item
2229	OAB-q (1-week recall)
2229	OverActive Bladder questionnaire (1-week recall)
2230	FM-PBC
2230	Family Member Perception of Bladder Condition
2231	FACT-PSI
2231	Functional Assessment of Cancer Therapy - Pulmonary Symptom Index
2232	Shortened HS-FOCUS - Parent version
2232	Hunter Syndrome-Functional Outcomes for Clinical Understanding Scale - Shortened version - Parent version
2233	PP-NRS
2233	Peak Pruritus Numerical Rating Scale
2234	Berlin Questionnaire
2234	Berlin Questionnaire

2235	QoL-Q Diabetes
2235	Diabetes Quality of Life Questionnaire
2236	OAB-SAT-q
2236	OverActive Bladder Satisfaction with Treatment Questionnaire
2237	UGDS-M
2237	Utrecht Gender Dysphoria Scale - Male version
2238	CBOCI
2238	Clark-Beck Obsessive-Compulsive Inventory
2239	PSS
2239	Psoriasis Symptom Scale
2240	IBS-D daily symptom diary and event log
2240	Irritable bowel syndrome-diarrhea daily symptom diary and event log
2241	NFPSI-17
2241	National Comprehensive Cancer Network Functional Assessment of Cancer Therapy - Prostate Symptom Index
2242	DSAS-2
2242	Type 2 Diabetes Stigma Assessment Scale
2243	NFBrSI-24
2243	National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy - Brain Symptom Index
2244	OAB-FIM
2244	OverActive Bladder - Family Impact Measure
2245	FACT-LCS
2245	Functional Assessment of Cancer Therapy - Lung Cancer Subscale
2246	BSS
2246	Beck Scale for Suicide Ideation
2247	BHS
2247	Beck Hopelessness Scale
2248	NFLSI-17
2248	National Comprehensive Cancer Network-Functional Assessment of Cancer Therapy - Lung Symptom Index (17-items)
2249	FOSI
2249	Functional Assessment of Cancer Therapy - Ovarian Symptom Index

2250	GME-Q
2250	Glucose Monitoring Experiences Questionnaire
2251	PQATv2
2251	Patient’s Qualitative Assessment of Treatment version 2
2252	FLSI-12
2252	Functional Assessment of Cancer Therapy - Lung Symptom Index
2253	BAT
2253	Bladder Assessment Tool
2254	OPAQ
2254	Osteoporosis Assessment Questionnaire
2255	PACIS
2255	Perceived Adjustment to Chronic Illness Scale
2256	PC-QoL
2256	Prostate Cancer Quality of Life scale
2257	PDI
2257	Psychological Distress Inventory
2258	PDQL
2258	Parkinson's Disease Quality of Life Questionnaire
2259	PFSDQ
2259	Pulmonary Functional Status & Dyspnea Questionnaire
2260	PGC Morale Scale
2260	Philadelphia Geriatric Center Morale Scale
2261	PGWBI
2261	Psychological General Well-Being Index
2262	MOS-SSS
2262	Medical Outcomes Study (MOS) Social Support Survey
2263	MPQ
2263	McGill Pain Questionnaire
2264	NEQ
2264	Needs Evaluation Questionnaire
2265	ODI

2265	Oswestry Disability Index
2266	PAIS/PAIS-SR
2266	Psychosocial Adjustment to Illness Scale
2267	Patient-Specific Index
2268	MPAC
2268	Memorial Pain Assessment Card
2269	MSAS
2269	Memorial Symptom Assessment Scale
2270	MSQ Version 2.1
2270	Migraine-Specific Quality-of-Life Questionnaire
2271	NDI
2271	Neck Disability Index
2272	OHIP/OHIP-14
2272	Oral Health Impact Profile
2273	PDQ-39
2273	Parkinson’s Disease Questionnaire - 39
2274	PGI
2274	Patient Generated Index
2275	MQOL-HIV
2275	Multidimensional Quality of Life questionnaire for HIV/AIDS
2276	NDII
2276	Neck Dissection Impairement Index
2277	NIH-CPSI
2277	National Institute of Health Chronic Prostatitis Symptom Index
2278	NEST
2278	Needs at the End-of-Life Screening Tool
2279	OARS
2279	Older Americans Resources and Services Multidimensional Functional Assessment Questionnaire
2280	OSDI
2280	Ocular Surface Disease Index
2281	NPS

2281	Neuropathic Pain Scale
2282	PAQLQ
2282	Paediatric Asthma Quality of Life Questionnaire
2283	PedsQL Generic Core Scales
2283	Pediatric Quality of Life Inventory Generic Core Scales
2284	Peds FAACT
2284	Pediatric Functional Assessment of Anorexia Cachexia
2285	TSD-OC
2285	SIO Obesity-Related Disability Test
2286	FACT-VCI
2286	FACT-Bl-Cys
2286	Functional Assessment of Cancer Therapy - Vanderbilt Cystectomy Index
2286	Functional Assessment of Bladder Cancer – Bladder Cystectomy
2287	FACT-Th18
2287	Functional Assessment of Cancer Therapy - Thrombocytopenia (18-item version)
2288	HDSS
2288	Hyperhidrosis Disease Severity Scale
2289	PROMIS Pediatric Bank v1.0 Sleep Disturbance
2289	Patient-Reported Outcomes Information System Pediatric Bank v1.0 Sleep Disturbance
2290	PROMIS Pediatric SF8 v1.0 SRI
2290	Patient-Reported Outcomes Information System Pediatric Short Form v1.0 Sleep-Related Impairment 8a
2291	PROMIS Short Form v1.0 Sleep Disturbance 8b
2291	Patient-Reported Outcomes Information System Short Form v1.0 Sleep Disturbance 8b
2292	FACT-Th11
2292	Functional Assessment of Cancer Therapy - Thrombocytopenia (11-item version)
2293	MSA-QoL
2293	Multiple System Atrophy health-related Quality of life scale
2294	CBI
2294	Caregiver Burden Inventory
2295	QDIS-MCC
2295	Quality of Life Disease Impact Scale–Multiple Chronic Conditions form

2296	Care-ILI-QoL
2296	QoL of CAREgivers of children with Influenza-Like Illness
2297	Neuro-QoL Item Bank v1.0 – Upper Extremity Function – Fine Motor, ADL
2297	Quality of Life in Neurological Disorders Item bank v1.0 – Upper Extremity Function – Fine Motor, ADL
2298	JOACMEQ
2298	Japanese Orthopaedic Association Cervical Myelopathy Evaluation Questionnaire
2299	SF-NDI
2299	Short Form Nepean Dyspepsia Index
2300	PBI-W
2300	Patient Benefit Index - Chronic Wounds
2301	PBI-UAW
2301	Patient Benefit Index - Chronic Wounds, special version for evaluation of Ultrasound treatment
2302	PBI-K
2302	Patient Benefit Index - Cosmetic indications
2303	PBI-L
2303	Patient Benefit Index - Lymphedema
2304	PACS
2304	Penn Alcohol Craving Scale
2305	CLDQ-HCV
2305	Chronic Liver Disease Questionnaire - Hepatitis C Version
2306	QOL-B v3.1
2306	Quality of Life Questionnaire - Bronchiectasis v3.1
2307	FAHI
2307	Functional Assessment of Human Immunodeficiency Virus Infection
2308	FACT-N
2308	Functional Assessment of Cancer Therapy-Neutropenia
2309	COmprehensive Score for financial Toxicity
2310	PRAI
2310	Patient-Reported Arthralgia Inventory
2311	CAMPHOR Utility Index
2311	Cambridge Pulmonary Hypertension Outcome Review Utility Index

2312	PROMIS Bank v1.0 SRI
2312	Patient-Reported Outcomes Information System Bank v1.0 Sleep-Related Impairment
2313	PROMIS Pediatric SF8 v1.0 Sleep Disturbance
2313	Patient-Reported Outcomes Information System Pediatric Short Form v1.0 Sleep Disturbance 8a
2314	PROMIS Pediatric Bank v1.0 SRI
2314	Patient-Reported Outcomes Information System Pediatric Bank v1.0 Sleep-Related Impairment
2315	PROMIS Pediatric SF4 v1.0 SRI
2315	Patient-Reported Outcomes Information System Pediatric Short Form v1.0 Sleep-Related Impairment 4a
2316	PROMIS Short Form v1.0 Sleep Disturbance 4a
2316	Patient-Reported Outcomes Information System Short Form v1.0 Sleep Disturbance 4a
2317	QDIS-7-item scale
2317	Quality of Life Disease Impact Scale–7 item scale
2318	QDIS-CAT
2318	Quality of Life Disease Impact Scale–Computerized Adaptive Testing form
2319	PADQOL
2319	Peripheral Artery Disease Quality of Life Questionnaire
2320	Peds FAACT-10
2320	Pediatric Functional Assessment of Anorexia Cachexia - 10
2321	SKINDEX-16 for AA
2321	SKINDEX-16 for Alopecia Areata
2322	ItchyQoL - Bother version
2322	ItchyQoL - Bother version
2323	PBI-POD
2323	Patient Benefit Index - Peripheral artery Occlusive Disease
2324	PBI-MS
2324	Patient Benefit Index - Multiple Sclerosis
2325	P-FIBS
2325	Pain Frequency, Intensity, and Burden Scale
2326	Wound-QoL
2326	Wound-QoL questionnaire
2327	STOP-Bang questionnaire

2327	Snoring, Tiredness during daytime, Observed apnea, and high blood Pressure (P) combined with Bang–BMI questionnaires
2328	RLCST
2328	Recent Life Change Stress Test
2329	SCS
2329	Site of Care Satisfaction
2330	Peds FACIT-F
2330	Pediatric Functional Assessment of Chronic Illness Therapy - Fatigue
2331	FACIT-TS-PS
2331	Functional Assessment of Chronic Illness Therapy - Treatment Satisfaction - Patient Satisfaction
2332	FACT-B + 4
2332	Functional Assessment of Cancer Therapy - Breast Cancer + Arm subscale
2333	PROMIS Bank v1.0 Sleep Disturbance
2333	Patient-Reported Outcomes Information System Bank v1.0 Sleep Disturbance
2334	PROMIS Short Form v1.0 Sleep Disturbance 8a
2334	Patient-Reported Outcomes Information System Short Form v1.0 Sleep Disturbance 8a
2335	PROMIS Short Form v1.0 Sleep-Related Impairment 4a
2335	Patient-Reported Outcomes Information System Short Form v1.0 Sleep-Related Impairment 4a
2336	PROMIS Pediatric SF4 v1.0 Sleep Disturbance
2336	Patient-Reported Outcomes Information System Pediatric Short Form v1.0 Sleep Disturbance 4a
2337	PROMIS Short Form v1.0 Sleep Disturbance 6a
2337	Patient-Reported Outcomes Information System Short Form v1.0 Sleep Disturbance 6a
2338	PROMIS Short Form v1.0 Sleep-Related Impairment 8a
2338	Patient-Reported Outcomes Information System Short Form v1.0 Sleep-Related Impairment 8a
2339	PQoL Carers
2339	Parkinsonism Carers Quality of Life
2340	QDIS-1-item
2340	Quality of Life Disease Impact Scale–1 global impact item
2341	BFAS
2341	Baylor Functional Assessment Scale
2342	PROMIS-Fatigue MS
2342	Patient-Reported Outcomes Measurement Information System-Fatigue Multiple Sclerosis

2343	SPID
2343	Sum of Pain Intensity Differences
2344	QOL-RA Scale
2344	Quality of Life-Rheumatoid Arthritis Scale
2345	QOLVFQ
2345	Quality of Life and Vision Function Questionnaire
2346	QOLS
2346	Quality of Life Scale
2347	RhinQLQ
2347	Rhinitis Quality of Life Questionnaire
2348	SCB
2348	Screen for Caregiver Burden
2349	SCI
2349	Subjective Chemotherapy Impact scale
2350	SFI
2350	Sexual Function Index
2351	QOLIE-89
2351	Quality of Life in Epilepsy Inventory-89
2352	QQ-q
2352	Q(uality)-Q(uantity) questionnaire
2353	QWB-SA
2353	Quality of Well-Being scale Self-Administered
2354	RFIPC
2354	Rating Form of IBD Patient Concerns
2355	RSCL
2355	Rotterdam Symptom Checklist
2356	FDDQL
2356	Quality of Life Questionnaire for Functional Digestive Disorders
2357	QPD-32
2357	Questionnaire for Peptic Disease-32 items
2358	Qual-OT

2358	Quality of Life in Occupational Therapy
2359	Reflux-Qual
2359	Quality of Life Questionnaire in Gastroesophageal Reflux
2360	RQLQ
2360	Rhinoconjunctivitis Quality of Life Questionnaire
2361	RSVP
2361	Refractive Status and Vision Profile
2362	SAQ
2362	Seattle Angina Questionnaire
2363	ZungSAS
2363	Zung Self-rating Anxiety Scale
2364	SAT-P
2364	Satisfaction profile
2365	SCFS-6
2365	Schwartz Cancer Fatigue Scale
2366	SCNS
2366	Supportive Care Needs Survey
2367	SDS
2367	Symptom Distress Scale
2368	AQoL
2368	Assessment of Quality of Life
2369	Artemis
2369	Assessment of Quality of Life in lower limb arteriopathy
2370	ARTQ
2370	Attitudes to Randomised Clinical Trials Questionnaire
2371	ASC
2371	Asthma Symptom Checklist
2372	ASES
2372	Asthma Self-Efficacy Scale
2373	ATD-PA
2373	Assistive Technology Device Predisposition Assessment

2374	ASUI
2374	Asthma Symptom Utility Index
2375	AUQUEI
2375	Pictured Child’s Quality of Life Self Questionnaire
2376	AUSCAN
2376	Australian/Canadian Osteoarthritis Hand Index
2377	VHQ
2377	Vertigo Handicap Questionnaire
2378	VSS
2378	Vertigo Symptom Scale
2379	AVVQ
2379	Aberdeen Varicose Veins Questionnaire
2380	W-BQ
2380	Well-Being Questionnaire
2381	WHOQOL-100
2381	World Health Organization Quality of Life assessment instrument
2382	WHQ
2382	Women’s Health Questionnaire
2383	EORTC QLQ-LMC21
2383	EORTC Quality of Life Questionnaire - Liver Metastases Colorectal Module
2384	ASES
2384	Arthritis Self-Efficacy Scale
2385	BPFS
2385	Back Pain Functional Scale
2386	OxAFQ-C
2386	The Oxford Ankle Foot Questionnaire for Children
2387	MFPDI
2387	The Manchester Foot Pain Disability Index
2388	Improved HAQ
2388	Improved Health Assessment Questionnaire
2389	FACT-GOG-NTX12

2389	Functional Assessment of Cancer Therapy - Gynecologic Oncology Group-Neurotoxicity 12
2390	FACT-GOG-NTX4
2390	Functional Assessment of Cancer Therapy - Gynecologic Oncology Group-Neurotoxicity 4
2391	IBS-SSS
2391	Irritable Bowel Syndrome Severity Scoring System
2392	PKU-QOL
2392	Phenylketonuria impact and treatment Quality Of Life Questionnaire
2393	WPS-RA
2393	Rheumatoid arthritis-specific Work Productivity Survey
2394	Arthritis Impact Measurement Scale
2395	Fatigue Assessment Scale
2396	SEI
2396	Smoking Effects Inventory
2397	OR-SDS
2397	Opioid-Related Symptom Distress Scale
2398	NMSQuest
2398	Non-motor Symptoms Questionnaire
2399	FACIT
2399	Functional Assessment of Chronic Illness Therapy Measurement System
2400	HWBI
2400	Hemophilia Well-Being Index
2401	PedsQL Neuromuscular Module
2401	Pediatric Quality of Life Inventory Neuromuscular Module
2402	FACT-Hep
2402	Functional Assessment of Cancer Therapy - Hepatobiliary Cancer
2403	PEESS v2.0
2403	Pediatric Eosinophilic Esophagitis Symptom Severity Module, version 2.0
2404	CFQ-R
2404	Cystic Fibrosis Questionnaire-Revised
2405	TSS
2405	Total Symptom Score

2406	LASA or CLAS
2406	Linear Analogue Self-Assessment or Cancer Linear Analog Scale
2407	PBAC
2407	Pictorial Blood-loss Assessment Chart
2408	FAMS
2408	Functional Assessment of Multiple Sclerosis
2409	E-RS
2409	Evaluating Respiratory Symptoms
2410	CFRSD
2410	Cystic Fibrosis Respiratory Symptom Diary
2411	HIGH-C
2411	Hypomania Interview Guide (Including Hyperthymia) – Current Assessment (Interview Version)
2412	FACT-Lym
2412	Functional Assessment of Cancer Therapy - Lymphoma
2413	ADEOS
2413	ADherence Evaluation of OSteoporosis treatment
2414	VSRQ
2414	Visual Simplified Respiratory Questionnaire
2415	VVSymQ
2415	Varicose Veins Symptoms Questionnaire
2416	BASIQ
2416	Brain Metastases Symptom and Impact Questionnaire
2417	BASC
2417	Brief Assessment Scale for Caregivers
2418	UDI-6
2418	Urogenital Distress Inventory - Short Form
2419	MEQ-REV-SA
2419	Morningness Eveningness Questionnaire, Revised (Self-Assessment Version)
2420	PDQ
2420	Peyronie’s Disease Questionnaire
2421	AWS

2421	Arthritis-Work Spillover Scale
2422	FRI Index
2422	Functional Reading Independence Index
2423	EDSQ
2423	Eye-Drop Satisfaction Questionnaire
2424	Bt-DUX
2424	DUX Questionnaire for lower extremity bone tumor
2425	ISI
2425	Insomnia Severity Index
2426	NFLymSI-18
2426	National Comprehensive Cancer Network Functional Assessment of CancerTherapy - Lymphoma Symptom lndex-18
2427	AIDAI
2427	Autoinflammatory diseases Activity Index Diary
2428	BQ Back Pain
2428	Bournemouth Questionnaire - Back Pain
2429	ATAQ Adult
2429	Asthma Therapy Assessment Questionnaire Adult
2430	Anxiety Inventory for Respiratory disease
2431	ESS-CHAD
2431	Epworth Sleepiness Scale - Child Adolescent
2432	VASCUQOL
2432	Vascular Quality of Life Questionnaire
2433	TSS
2433	Patient and Partner Treatment Satisfaction Scale in Erectile Dysfunction
2434	EORTC QLQ-EN24
2434	EORTC Quality of Life Questionnaire - Endometrial Cancer Module
2435	ICOAP-Hip
2435	Intermittent and Constant Osteoarthritis Pain - Hip version
2436	EORTC QLQ-STO22
2436	EORTC Quality of Life Questionnaire - Gastric Cancer Module
2437	FFMQ

2437	Five Facet Mindfulness Questionnaire
2438	EORTC QLQ-ELD14
2438	EORTC Quality of Life Questionnaire - Elderly Cancer Patients Module
2439	EORTC QLQ-GINET21
2439	EORTC Quality of Life Questionnaire - Neuroendocrine Carcinoid Module
2440	EORTC QLQ-OES18
2440	EORTC Quality of Life Questionnaire - Oesophageal Cancer Module
2441	DRSP
2441	Daily Record of Severity of Problems
2442	ZBPI
2442	Zoster Brief Pain Inventory
2443	IES
2443	Impact of Event Scale
2444	SAT-37
2444	Satisfaction with Care Scale
2445	RPSQ
2445	Recent Physical Symptoms Questionnaire
2446	Trauma Questionnaire
2446	Trauma Questionnaire
2447	SPS-13
2447	13-item Stanford Presenteeism Scale
2448	PedsQL Healthcare Satisfaction Generic Module
2448	Pediatric Quality of Life Inventory Healthcare Satisfaction Generic Module
2449	CASA-Q
2449	Cough And Sputum Assessment Questionnaire
2450	MIQ
2450	Menorrhagia Impact Questionnaire
2451	PBI-S
2451	Patient Benefit Index - Standard
2452	SDS
2452	The Zung Self-rating Depression Scale

2453	MOxFQ
2453	The Manchester-Oxford Foot Questionnaire
2454	EORTC QLQ-INFO25
2454	EORTC Quality of Life Questionnaire - Information Module
2455	FACT-Leu
2455	Functional Assessment of Cancer Therapy - Leukemia
2456	FACT-GOG-NTX13
2456	Functional Assessment of Cancer Therapy - Gynecologic Oncology Group-Neurotoxicity 13
2457	MCQ
2457	Mild Cognitive Impairment Questionnaire
2458	ARCI-49
2458	Addiction Research Center Inventory 49 check-list
2459	ASAS 20/40/50/70
2459	Assessment in Ankylosing Spondylitis response criteria
2460	FBDSI
2460	Functional Bowel Disorder Severity Index
2461	CD-QOL
2461	Celiac Disease Quality of Life Measure
2462	EORTC QLQ-CLL17
2462	EORTC Quality of Life Questionnaire - Chronic Lymphocytic Leukaemia Module
2463	PedsQL Pediatric Present Functioning Visual Analogue Scales
2463	Pediatric Quality of Life Inventory Pediatric Present Functioning Visual Analogue Scales
2464	AS-AIMS2
2464	Ankylosing Spondylitis Arthritis Impact Measurement Scales 2
2465	IPE
2465	Index of Premature Ejaculation
2466	mBPI-e
2466	Modified Brief Pain Inventory-exploratory form
2467	PPSM
2467	Patient Perception of Study Medication
2468	TSQ-G

2468	Treatment Satisfaction Questionnaire for Gastro-oesophageal reflux disease
2469	MSTCQ
2469	Multiple Sclerosis Treatment Concerns Questionnaire
2470	Parkinson Fatigue Scale
2471	Haemo-QOL
2471	Haemophilia Quality of Life Questionnaire for Children
2472	CHES-Q
2472	Current Health Satisfaction Questionnaire
2473	EORTC QLQ-OG25
2473	EORTC Quality of Life Questionnaire - Oesophago-Gastric Module
2474	KSADS-COMP - Self-administered (for Youth)
2474	Kiddie Schedule for Affective Disorders and Schizophrenia - Computerized versions - Self-administered (for Youth)
2475	FBI
2475	Fibromyalgia Bladder Index
2476	OAB-S
2476	Overactive Bladder Satisfaction Questionnaire version 3.0
2477	ODQ
2477	Oxford Depression Questionnaire
2478	Kamath and Stothard Questionnaire
2478	Kamath and Stothard Questionnaire
2479	UTISA
2479	Urinary Tract Infection Symptom Assessment
2480	AIA
2480	Activity Impairment Assessment
2481	OMDQ
2481	Oral Mucositis Daily Questionnaire
2482	Exacerbation of Chronic Pulmonary Disease Tool
2483	MTWS
2483	Minnesota Tobacco Withdrawal Scale
2484	MiniPAQLQ
2484	Mini Paediatric Asthma Quality of Life Questionnaire

2485	UC-CD Health Status
2485	Ulcerative Colitis and Crohn's Disease Health Status Scales
2486	BACRI
2486	Bristol-Myers Anorexia/Cachexia Recovery Instrument
2487	SPS-6
2487	6-item Stanford Presenteeism Scale
2488	CMCQ
2488	Comorbid Medical Conditions Questionnaire
2489	FQ
2489	Fear Questionnaire
2490	AAV-PRO
2490	ANCA-Associated Vasculitis Patient-Reported Outcomes
2491	PedsQL Healthcare Satisfaction Hematology/Oncology Specific Module
2491	Pediatric Quality of Life Inventory Healthcare Satisfaction Hematology/Oncology Specific Module
2492	AAQ
2492	Animated Activity Questionnaire
2493	PedsQL Pediatric Pain Coping Inventory
2493	Pediatric Quality of Life Inventory Pediatric Pain Coping Inventory
2494	PEP
2494	Premature Ejaculation Profile
2495	AIMS2-SF
2495	Arthritis Impact Measurement Scales 2-Short form
2496	TSS-IOP
2496	Treatment Satisfaction Survey for Intraocular Pressure
2497	OPSAT-Q
2497	Osteoporosis Patient Satisfaction Questionnaire
2498	Haem-A-QoL
2498	Haemophilia Quality of Life Questionnaire for Adults
2499	CHO-KLAT
2499	Canadian Hemophilia Outcomes - Kids' Life Assessment Tool
2500	CDI

2500	CDI 2
2500	Children's Depression Inventory
2501	LupusQoL
2501	Lupus Quality Of Life
2502	HRPQ
2502	Health Related Productivity Questionnaire
2503	CBCL
2503	Child Behavior Checklist
2504	FTFQ
2504	First Time Fathers Questionnaire
2505	HPN-QoL
2505	Home Parenteral Nutrition - Quality of Life
2506	Sec QoL
2506	Spanish society of contraception quality-of-life
2507	FertiQoL
2507	Fertility Quality of Life
2508	FPI
2508	Fertility Problem Inventory
2509	CarGOQoL
2509	CareGiver Oncology Quality of Life questionnaire
2510	SNOT
2510	Sino-Nasal Outcome Test
2511	SIS
2511	Sheehan Irritability Scale
2512	BES
2512	Binge Eating Scale
2513	VPS
2513	Vitality Plus Scale
2514	NFKSI-19
2514	National Comprehensive Cancer Network Functional Assessment of Cancer Therapy - Kidney Symptom Index 19
2515	VSSS

2515	Verona Service Satisfaction Scale
2516	VECS
2516	Verona Expectations for Care Scale
2517	OPQOL
2517	Older People's Quality of Life
2518	EES-C
2518	Emotional Eating Scale in Children and Adolescents
2519	MASQ
2519	Multiple Ability Self-Report Questionnaire
2520	QUIP
2520	Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease
2521	Mini-MASQ
2521	Mini-Mood and Anxiety Symptom Questionnaire
2522	URICA
2522	University of Rhode Island Change Assessment
2523	IWQOL-Lite-CT
2523	Impact of Weight on Quality of Life-Lite Clinical Trials Version
2524	SGRQ-C
2524	St George's Respiratory Questionnaire - COPD-Specific Version
2525	SR-MAD
2525	Self-Reported Misuse, Abuse, and Diversions of Prescription Opioids
2526	CPQ
2526	Chronic Pain Questions
2527	FKSI-10
2527	Functional Assessment of Cancer Therapy-Kidney Symptom Index
2528	COMPASS 31
2528	Composite Autonomic Symptom Score 31
2529	DIsability RElated to COPD Tool
2530	EARNS-Q
2530	The Experience with Allergic Rhinitis Nasal Spray Questionnaire
2531	S-STS

2531	Sheehan - Suicidality Tracking Scale
2532	SVS
2532	Stress Vulnerability Scale
2533	FGVS
2533	Freedom from Glasses Value Scale
2534	Short FES-I
2534	Short Falls Efficacy Scale-International
2535	COPD-PS
2535	COPD Population Screener
2536	S-QoL 41
2536	Schizophrenia Quality of Life Questionnaire – Clinical Research Form
2537	SIAQ
2537	Self-Injection Assessment Questionnaire
2538	FKSI-DRS
2538	Functional Assessment of Cancer Therapy- Kidney Symptom Index- Disease related Symptoms
2539	EBAS
2539	Environmental Barriers to Diabetes-regimen Adherence
2540	ThyPRO
2540	Thyroïd-specific patient reported outcome
2541	CFQ
2541	Cognitive Failures Questionnaire
2542	Manual-WIS
2542	Manual Work Instability Scale
2543	LATCH
2543	A breast feeding Charting System and Documentation Tool
2544	QUIP-RS
2544	Questionnaire for Impulsive-Compulsive Disorders in Parkinson’s Disease–Rating Scale
2545	WCQ
2545	Worthing Chemotherapy Questionnaire
2546	HIT-6
2546	Headache Impact Test

2547	OWS
2547	Office Work Screen
2548	Peds FACT-Br
2548	Pediatric Functional Assessment Of Cancer Therapy - Brain
2549	Duke-PH
2549	Duke Population Health Profile
2550	PASQ
2550	Pain Assessed Acromegaly Symptom Questionnaire
2551	WHGQ
2551	Women’s Hair Growth Questionnaire
2552	FSIQ-RMS
2552	Fatigue Symptoms and Impacts Questionnaire - Relapsing Multiple Sclerosis
2553	KIMS
2553	Kentucky Inventory of Mindfulness Skills
2554	HIGH-C-SR
2554	Hypomania Interview Guide (Including Hyperthymia) – Current Assessment (Self-Rating Version)
2555	IIQ-7
2555	Incontinence Impact Questionnaire - Short Form
2556	EI
2556	TFEQ
2556	Eating Inventory
2556	Three-Factor Eating Questionnaire
2557	ICSI-ICPI
2557	Interstitial Cystitis Symptom Index and Problem Index
2558	FAIT-U
2558	Functional Assessment of Incontinence Therapy - Urinary
2559	FAIT-F
2559	Functional Assessment of Incontinence Therapy - Fecal
2560	BILD
2560	Brief Index of Lupus Damage
2561	FES-I

2561	Falls Efficacy Scale-International
2562	SOWS
2562	Subjective Opiate Withdrawal Scale
2563	S-QOL 18
2563	Schizophrenia Quality of Life Questionnaire Short Form – Clinical Practice
2564	S-CGQoL
2564	Schizophrenia CareGiver Quality of Life Questionnaire
2565	EES
2565	Emotional Eating Scale
2566	LDQOL
2566	Liver Disease Quality of Life Questionnaire
2567	LDSI
2567	Liver Disease Symptom Index
2568	ISE
2568	Infertility Self-Efficacy scale
2569	SQLS
2569	Schizophrenia Quality of Life Scale
2570	MASQ-SF
2570	Mood and Anxiety Symptom Questionnaire - Short Form
2571	ID-Pain
2571	IDentification Pain questionnaire
2572	FSDS-R
2572	Female Sexual Distress Scale – Revised
2573	BCI
2573	Bladder Cancer Index
2574	Skindex-29+3
2574	3 Cutaneous Lupus Erythematosus items complementing the Skindex 29
2575	VA LV VFQ-48
2575	Veterans Affairs Low-Vision Visual Functioning Questionnaire
2576	FCI
2576	Functional Comorbidity Index

2577	FCQ
2577	Frankfurt Complaint Questionnaire
2578	GOHAI
2578	Geriatric Oral Health Assessment Index
2579	Hemo-Sat
2579	Hemophilia Patient Satisfaction Scale
2580	Hatoum's sleep Questionnaire
2580	Hatoum's sleep Questionnaire
2581	SOAPP-12
2581	Screener and Opioid Assessment for Patients with Pain – 12-item version
2582	OSES
2582	Opioid Side Effects Scale
2583	HoMASQ
2583	Home Monitoring Acceptance and Satisfaction Questionnaire
2584	HO Scale
2584	Cook-Medley Hostility (Ho) scale
2585	SAL
2585	Sexual Activity Log
2586	IADCQ
2586	Impact of Alzheimer's Disease on Caregiver Questionnaire
2587	PBQ
2587	Patient Benefit Questionnaire
2588	PDS
2588	Personal Distress Scale
2589	SNAP-ADHD
2589	Swanson, Nolan, and Pelham Rating Scale for ADHD
2590	SexFX Female version
2590	Sex Effects scale Female version
2591	STAR
2591	Soft Tissue Anesthesia Recovery
2592	PUQE

2592	Pregnancy-Unique Quantification of Emesis
2593	WHYMPI
2593	West Haven - Yale Multidimensional Pain Inventory
2594	WIQ
2594	Walking Impairment Questionnaire
2595	WLQ
2595	Work Limitations Questionnaire
2596	WOMAC
2596	Western Ontario and McMaster Universities Arthritis Index
2597	WOOS
2597	Western Ontario Osteoarthritis of the Shoulder index
2598	WORC
2598	Western Ontario Rotator Cuff index
2599	SWED-QUAL
2599	Swedish Health-Related Quality of Life Survey
2600	SWN
2600	Subjective Well-being under Neuroleptic treatment
2601	TAAQOL
2601	TNO-AZL Questionnaire for Adult's Health-related Quality of Life
2602	TedQL
2602	Quality of Life measure for children aged 3-8 years
2603	TIQ
2603	Therapy Impact Questionnaire
2604	UCLA-DQ
2604	UCLA Dizziness Questionnaire
2605	UCLA-PCI
2605	UCLA Prostate Cancer Index
2606	UCLA-PCI-SF
2606	UCLA Prostate Cancer Index Short Form
2607	UROLIFE
2607	BPHQoL9

2607	Benign Prostatic Hypertrophy Health-Related Quality of Life Questionnaire
2608	UW-QOL
2608	University of Washington Quality of Life Instruments
2609	CAP-Sym
2609	Community-Acquired Pneumonia Symptom questionnaire
2610	Subjective Health Estimations
2611	SIP
2611	Sickness Impact Profile
2612	SODA
2612	Severity of Dyspepsia Assessment
2613	SLQQ
2613	Sexual Life Quality Questionnaire
2614	SOLQ
2614	Seattle Obstructive Lung Disease Questionnaire
2615	SQLP
2615	Subjective Quality of Life Profile
2616	SS-QOL
2616	Stroke-Specific Quality Of Life measure
2617	SSS-30
2617	SSS-15
2617	SSS-RES
2617	Service Satisfaction Scale
2618	UAS-TD
2618	Urticaria Activity Score - Twice Daily
2619	DAS-SF
2619	Diabetes Acceptance Scale - Short Form
2620	AFQ-Y
2620	Avoidance and Fusion Questionnaire for Youth
2621	VQIDS-SR5
2621	The Very Quick Inventory of Depressive Symptomatology
2622	Neuro-QoL Item Bank v1.0 - Emotional and Behavioral Dyscontrol

2622	Quality of Life in Neurological Disorders Item Bank v1.0 - Emotional and Behavioral Dyscontrol
2623	Neuro-QoL Item Bank v1.0 - Fatigue
2623	Quality of Life in Neurological Disorders Item Bank v1.0 - Fatigue
2624	Neuro-QoL Item Bank v1.0 - Pediatric Social Relationships - Interaction With Peers
2624	Quality of Life in Neurological Disorders Item Bank v1.0 – Pediatric Social Relationships - Interaction With Peers
2625	Neuro-QoL Item Bank v1.0 - Pediatric Stigma
2625	Quality of Life in Neurological Disorders Item Bank v1.0 – Pediatric Stigma
2626	MWQ
2626	Munich Wrist Questionnaire
2627	Neuro-QoL Item Bank v1.1 - Satisfaction With Social Roles and Activities
2627	Quality of Life in Neurological Disorders Item Bank v1.1 - Satisfaction With Social Roles and Activities
2628	Neuro-QoL Item Bank v2.0 - Pediatric Cognitive Function
2628	Quality of Life in Neurological Disorders Item Bank v2.0 - Pediatric Cognitive Function
2629	IOF-wrist fracture questionnaire
2629	International Osteoporosis Foundation wrist fracture questionnaire
2630	PASQoL
2630	Postanaesthesia Short-term Quality of Life tool
2631	Neuro-QoL Scale v1.0 - Communication
2631	Quality of Life in Neurological Disorders Scale v1.0 - Communication
2632	Neuro-QoL Scale v1.1 - Pediatric Lower Extremity
2632	Quality of Life in Neurological Disorders Scale v1.1 - Pediatric Lower Extremity
2633	Neuro-QoL Scale v2.0 - HDQLIFE - End of Life Planning
2633	Quality of Life in Neurological Disorders Scale v2.0 - HDQLIFE - End of Life Planning
2634	CAMM
2634	Child and Adolescent Mindfulness Measure
2635	Neuro-QoL Bank v1.0 - Anxiety
2635	Quality of Life in Neurological Disorders Bank v1.0 - Anxiety
2636	Neuro-QoL Short Form v1.0 - Emotional and Behavioral Dyscontrol
2636	Quality of Life in Neurological Disorders Short Form v1.0 - Emotional and Behavioral Dyscontrol
2637	Neuro-QoL Item Bank v1.1 - Pediatric Depression

2637	Quality of Life in Neurological Disorders Item Bank v1.1 – Pediatric Depression
2638	Neuro-QoL Short Form v2.1 - Pediatric Fatigue
2638	Quality of Life in Neurological Disorders Short Form v2.1 - Pediatric Fatigue
2639	Neuro-QoL Short Form v2.0 - Cognitive Function
2639	Quality of Life in Neurological Disorders Short Form v2.0 - Cognitive Function
2640	Neuro-QoL Short Form v1.1 - Satisfaction with Social Roles and Activities
2640	Quality of Life in Neurological Disorders Short Form v1.1 - Satisfaction with Social Roles and Activities
2641	Neuro-QoL Short Form v1.0 - Positive Affect and Well-Being
2641	Quality of Life in Neurological Disorders Short Form v1.0 - Positive Affect and Well-Being
2642	Neuro-QoL Short Form v1.0 - Sleep Disturbance
2642	Quality of Life in Neurological Disorders Short Form v1.0 - Sleep Disturbance
2643	Neuro-QoL Short Form v2.0 - HDQLIFE - Concern with Death and Dying 6a
2643	Quality of Life in Neurological Disorders Short Form v2.0 - HDQLIFE - Concern with Death and Dying 6a
2644	Neuro-QoL Short Form v2.0 - HDQLIFE - Chorea 6a
2644	Quality of Life in Neurological Disorders Short Form v2.0 - HDQLIFE - Chorea 6a
2645	Neuro-QoL Short Form v2.0 - HDQLIFE - Swallowing Difficulties 6a
2645	Quality of Life in Neurological Disorders Short Form v2.0 - HDQLIFE - Swallowing Difficulties 6a
2646	Neuro-QoL Short Form v2.0 - HDQLIFE - Speech Difficulties 6a
2646	Quality of Life in Neurological Disorders Short Form v2.0 - HDQLIFE - Speech Difficulties 6a
2647	QGEN-8
2647	The Quality of Life General Form - 8-item
2648	CLEQoL
2648	Cutaneous Lupus Erythematosus Quality of Life
2649	QGEN-CAT
2649	The Quality of Life General Form - Computerized Adaptive Testing form
2650	DABS
2650	Derogatis Affects Balance Scale
2651	DABS-SF
2651	Derogatis Affects Balance Scale - Short Form
2652	DSP

2652	Derogatis Stress Profile
2653	CAHP
2653	Childhood Arthritis Health Profile
2654	Children's Arthritis Self-Efficacy
2655	CIJSS
2655	Chronic Illness Job Strain Scale
2656	AQ
2656	Aggression Questionnaire
2657	DEQ-5
2657	5-Item Dry Eye Questionnaire
2658	FROM-16
2658	Family Reported Outcome Measure
2659	ABS
2659	Aggressive Behavior Scale
2660	ASC-12
2660	Allodynia Symptom Checklist
2661	MAAS
2661	Mindful Attention Awareness Scale
2662	DSIS or DSIRS
2662	Daily Sleep Interference Scale or Daily Sleep Interference Rating Scale
2663	SIGH-SAD-SR
2663	Structured Interview Guide for the Hamilton Depression Rating Scale – Season Affective Disorder (Self-Rating Version)
2664	SCCAI
2664	Simple Clinical Colitis Activity Index
2665	DHI
2665	Duruöz Hand Index
2666	ICAF
2666	Combined Index of Severity of Fibromyalgia
2667	Skindex Mini
2667	Skindex Mini
2668	FSDS-DAO

2668	Female Sexual Distress Scale – Desire/Arousal/Orgasm
2669	Diabetes Acceptance Scale
2670	AAQ-II
2670	Acceptance and Action Questionnaire – II
2671	Block_DFE
2671	Block Folic Acid/Dietary Folate Equivalents Screener
2672	CD-PRO/SS
2672	Crohn's Disease Signs and Symptoms
2673	QIDS-SRD14
2673	14-item Quick Inventory of Depressive Symptomatology – Self Report - Daily
2674	UC-PRO/SS
2674	Ulcerative Colitis Signs and Symptoms
2675	Neuro-QoL Bank v2.0 - HDQLIFE - Concern with Death and Dying
2675	Quality of Life in Neurological Disorders Bank v2.0 - HDQLIFE - Concern with Death and Dying
2676	Neuro-QoL Bank v2.0 - HDQLIFE - Speech Difficulties
2676	Quality of Life in Neurological Disorders Bank v2.0 - HDQLIFE - Speech Difficulties
2677	Neuro-QoL Bank v2.0 - HDQLIFE - Chorea
2677	Quality of Life in Neurological Disorders Bank v2.0 - HDQLIFE - Chorea
2678	Neuro-QoL Item Bank v1.0 - Depression
2678	Quality of Life in Neurological Disorders Item Bank v1.0 - Depression
2679	Neuro-QoL Bank v2.0 - HDQLIFE - Swallowing Difficulties
2679	Quality of Life in Neurological Disorders Bank v2.0 - HDQLIFE - Swallowing Difficulties
2680	Neuro-QoL Item Bank v1.0 - Lower Extremity Function - Mobility
2680	Quality of Life in Neurological Disorders Item Bank v1.0 - Lower Extremity Function - Mobility
2681	Neuro-QoL Item Bank v1.0 - Positive Affect And Well-Being
2681	Quality of Life in Neurological Disorders Item Bank v1.0 – Positive Affect And Well-Being
2682	Neuro-QoL Item Bank v1.0 - Stigma
2682	Quality of Life in Neurological Disorders Item Bank v1.0 – Stigma
2683	Neuro-QoL Item Bank v2.0 - Cognitive Function
2683	Quality of Life in Neurological Disorders Item Bank v2.0 - Cognitive Function
2684	Neuro-QoL Item Bank v2.1 - Pediatric Fatigue

2684	Quality of Life in Neurological Disorders Item Bank v2.1 - Pediatric Fatigue
2685	Neuro-QoL Bank v1.0 - Ability To Participate In Social Roles and Activities
2685	Quality of Life in Neurological Disorders Bank v1.0 - Ability To Participate In Social Roles and Activities
2686	Neuro-QoL Short Form v1.0 - Ability to Participate in Social Roles and Activities
2686	Quality of Life in Neurological Disorders Short Form v1.0 - Ability to Participate in Social Roles and Activities
2687	Neuro-QoL Short Form v1.0 - Anxiety
2687	Quality of Life in Neurological Disorders Short Form v1.0 - Anxiety
2688	Neuro-QoL Short Form v1.0 - Depression
2688	Quality of Life in Neurological Disorders Short Form v1.0 - Depression
2689	Neuro-QoL Short Form v1.0 - Fatigue
2689	Quality of Life in Neurological Disorders Short Form v1.0 - Fatigue
2690	Neuro-QoL Short Form v1.0 - Lower Extremity Function - Mobility
2690	Quality of Life in Neurological Disorders Short Form v1.0 - Lower Extremity Function - Mobility
2691	Neuro-QoL Item Bank v1.0 - Pediatric Anxiety
2691	Quality of Life in Neurological Disorders Item Bank v1.0 – Pediatric Anxiety
2692	Neuro-QoL Short Form v1.0 - Pediatric Anxiety
2692	Quality of Life in Neurological Disorders Short Form v1.0 - Pediatric Anxiety
2693	Neuro-QoL Short Form v1.1 - Pediatric Depression
2693	Quality of Life in Neurological Disorders Short Form v1.1 - Pediatric Depression
2694	Neuro-QoL Short Form v1.0 - Pediatric Anger
2694	Quality of Life in Neurological Disorders Item Bank v1.0 – Pediatric Anger
2695	Neuro-QoL Short Form v2.0 - Pediatric Cognitive Function
2695	Quality of Life in Neurological Disorders Short Form v2.0 - Pediatric Cognitive Function
2696	Neuro-QoL Short Form v1.0 - Pediatric Pain
2696	Quality of Life in Neurological Disorders Short Form v1.0 - Pediatric Pain
2697	Neuro-QoL Short Form v1.0 - Pediatric Social Relationships - Interaction with Peers
2697	Quality of Life in Neurological Disorders Short Form v1.0 - Pediatric Social Relationships - Interaction with Peers
2698	Neuro-QoL Short Form v1.0 - Pediatric Stigma
2698	Quality of Life in Neurological Disorders Short Form v1.0 - Pediatric Stigma
2699	Neuro-QoL Short Form v1.0 - Stigma

2699	Quality of Life in Neurological Disorders Short Form v1.0 - Stigma
2700	QGEN-10
2700	The Quality of Life General Form - 10 item
2701	Haemo-QoL Index
2701	Haemophilia Quality of Life Questionnaire Index
2702	CSI
2702	Central Sensitization Inventory
2703	SWOG-QoL
2703	Southwest Oncology Group - Quality of life questionnaire
2704	vsSK-29
2704	vulvar-specific SKindex-29
2705	ESSPRI
2705	European League Against Rheumatism (EULAR) Sjögren syndrome Patient-Reported Index
2706	FPS
2706	Faces Pain Scale
2707	HIGH-R
2707	Hypomania Interview Guide (Including Hyperthymia) – Retrospective Assessment (Interview Version)
2708	CADI
2708	Cardiff Acne Disability Index
2709	EORTC QLQ-BLM30
2709	EORTC Quality of Life Questionnaire - Muscle Invasive Bladder Cancer
2710	MLCDP
2710	Major Life Changing Decision Profile
2711	BDHI
2711	Buss-Durkee Hostility Inventory
2712	T-QOL
2712	Teenager's Quality of Life Index
2713	PFI-14
2713	Psoriasis Family Index
2714	ASP
2714	Autonomic Symptom Profile

2715	FMI
2715	Freiburg Mindfulness Inventory
2716	CAMS-R 12-item version
2716	Cognitive and Affective Mindfulness Scale - Revised 12-item version
2717	SMQ
2717	Southampton Mindfulness Questionnaire
2718	VitiQoL
2718	Vitiligo-Specific Quality-of-Life Instrument
2719	VIS-22
2719	Vitiligo Impact Scale-22
2720	BQ Neck Pain
2720	Bournemouth Questionnaire - Neck Pain
2721	ASAT
2721	Addiction Severity Assessment Tool
2722	EORTC NMIBC-24
2722	EORTC Quality of Life Questionnaire - Non-Muscle-Invasive Bladder Cancer
2723	AFSS
2723	Atrial Fibrillation Severity Scale
2724	SGRQ
2724	St George’s Respiratory Questionnaire
2725	SI-MS
2725	Symptom Inventory for Multiple Sclerosis
2726	SIS v2.0
2726	Stroke Impact Scale & Stroke Toolbox
2727	SISC
2727	Structured Interview for Symptoms and Concerns
2728	SLQ
2728	Silver Lining Questionnaire
2729	SPFS
2729	Self-Perception of Female Sexuality
2730	SPI

2730	Symptom Problem Index
2731	STAI-AD
2731	State-Trait Anxiety Inventory-AD (Form Y)
2732	QOLI
2732	Quality of Life Inventory
2733	Qualeffo-41
2733	International Osteoporosis Foundation (IOF) Quality of Life questionnaire
2734	QUEST 2.0
2734	Quebec User Evaluation of Satisfaction with assistive Technology
2735	QWB
2735	Quality of Well Being scale
2736	RDS
2736	Rand 8-item Depression Screener
2737	RSDI
2737	Rhinosinusitis Disability Index
2738	RSUI
2738	Rhinitis Symptom Utility Index
2739	SCL-90-R
2739	Symptom Checklist-90-Revised
2740	SCSORF
2740	Santa Clara Strength of Religious Faith Questionnaire
2741	SEIQoL
2741	Schedule for the Evaluation of Individual Quality of Life
2742	SF-12
2742	SF-12v2
2742	SF-12 Health Survey
2743	SF-36
2743	SF-36v2
2743	SF-36 Health Survey
2744	SexFX Male version
2744	Sex Effects scale Male version

2745	NAPPA-QoL
2745	Nail Assessment in Psoriasis and Psoriatic Arthritis - Quality of Life
2746	NAPPA-PBI
2746	Nail Assessment in Psoriasis and Psoriatic Arthritis - Patient-relevant treatment benefits
2747	FACIT-Pal-14
2747	Functional Assessment of Chronic Illness Therapy - Palliative Care 14-item version
2748	MTSS
2748	Motivation To Stop Scale
2749	10-item ICD-QOL
2749	10-item Implantable Cardioverter Defibrillator Quality of Life Questionnaire
2750	15D
2750	15-dimensional health-related quality of life measure
2751	ABP
2751	Asthma Bother Profile
2752	ABPS
2752	Aberdeen Back Pain Scale
2753	ABS
2753	Affect Balance Scale
2754	ADI
2754	Acne Disability Index
2755	ADS
2755	Appraisal of Diabetes Scale
2756	AIDS-HAQ
2756	AIDS Health Assessment Questionnaire
2757	AIMS2
2757	Arthritis Impact Measurement Scales
2758	ALSAQ-40
2758	Amyotrophic Lateral Sclerosis Assessment Scales - 40 items
2759	AQLQ
2759	Asthma Quality of Life Questionnaire
2760	FACT-Th6

2760	Functional Assessment of Cancer Therapy - Thrombocytopenia (6-item version)
2761	GARS
2761	Groningen Activity Restriction Scale
2762	8-item ICD-QOL
2762	8-item Implantable Cardioverter Defibrillator-specific Quality of Life Questionnaire
2763	AAQ
2763	Attitudes to Asthma Questionnaire or Attitudes and Beliefs about Asthma
2764	AcroQoL
2764	Acromegaly Quality of Life questionnaire
2765	ADDQoL
2765	Audit of Diabetes Dependent QoL
2766	AdolRQLQ
2766	Adolescent Rhinoconjunctivitis Quality of Life Questionnaire
2767	ADQ
2767	Aberdeen Dyspepsia Questionnaire
2768	APQLQ
2768	Angina Pectoris Quality of Life Questionnaire
2769	AQ30
2769	AQ20
2769	Airways Questionnaire
2770	CQLQ
2770	Caregiver Quality Of Life Questionnaire (Physical & Emotional)
2771	FACT-Bl
2771	Functional Assessment of Cancer Therapy - Bladder cancer
2772	BIDR-16
2772	Balance Inventory of Desirable Responding - Short Form
2773	BARS
2773	Brief Adherence Rating Scale
2774	SCI-QOL
2774	Spinal Cord Injury – Quality of Life
2775	C-CAP1

2775	Cardiff Cardiac Ablation PROM - Pre-ablation
2776	RASP
2776	Relapse Assessment for Schizophrenia Patients
2777	FTS
2777	Facial Lines Treatment Satisfaction Questionnaire
2778	PGH-7 Child-Report Form
2778	PROMIS - Pediatric Global Health Child-Report Form
2779	PedsQL Diabetes Module 3.2
2779	Pediatric Quality of Life Inventory 3.2 Diabetes Module
2780	SMAQ
2780	Simplified Medication Adherence Questionnaire
2781	CFQoL
2781	Cystic Fibrosis Quality of Life
2782	PANAS
2782	Positive and Negative Affect Schedule
2783	Neuro-QOL SF
2783	Quality of Life in Neurological Disorders - Short forms
2784	PDQ-8
2784	Parkinson’s Disease Questionnaire - 8
2785	GRCQ
2785	Global Ratings of Change Questionnaire
2786	FCSI
2786	Functional Assessment of Cancer Therapy - Colorectal Cancer Symptom Index - 9 Item version
2787	LARS Score
2787	Low Anterior Resection Syndrome Score
2788	PROMIS-GH
2788	Patient-Reported Outcomes Measurement Information System - Global Health (Adult version)
2789	VASSPID
2789	Visual Analog Scale Sum of Pain Intensity Differences
2790	TOSS
2790	Total Ocular Symptom Score

2791	DHAFs
2791	Daily Health Assessment Forms
2792	Mini-International Neuropsychiatric Interview
2793	MDQ
2793	Menstrual Distress Questionnaire
2794	FES
2794	Family Environment Scale
2795	EORTC QLQ-C30
2795	EORTC Quality of Life Questionnaire - Core Questionnaire
2796	WAYS
2796	Ways of Coping Questionnaire
2797	DR-U
2797	Diabetic Retinopathy Utility instrument
2798	GlauCAT - Driving Scale
2798	Glaucoma Computerised Adaptive Test - Driving Scale
2799	Block 2005_OMFish
2799	Block 2005 Food Frequency Questionnaire - Omega 3/6
2800	CMHC-9
2800	Concise Mental Health Checklist-9
2801	CMHC
2801	Concise Mental Health Checklist
2802	BSRS-5R
2802	5-item Brief Symptom Rating Scale-Revised
2803	Block Alaska Supplemental
2803	Block Alaskan Food Supplemental Screener
2804	NSCLC-SAQ
2804	Non-small Cell Lung Cancer Symptom Assessment Questionnaire
2805	SMDDS
2805	Symptoms of Major Depressive Disorder Scale
2806	eq5d

Appendix 4.3: Composite measure search term list

Appendix 3. Composite measure search term list

id	names
0	MGC
0	Myasthenia Gravis Composite
1	cGVHD Symptom Scale
1	Lee Chronic Graft-versus-Host Disease Symptom Scale
2	mMRC
2	Modified Medical Research Council Dyspnea Scale
3	BOT-2
3	Bruininks-Oseretsky Test of Motor Proficiency Second Edition
4	PDAI
4	Perianal Disease Activity Index
5	CAADID
5	Conners' Adult ADHD Diagnostic Interview for DSM-IV
6	MDS-UPDRS
6	Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale
7	RLHQ
7	Reproductive Lifecycle and Hormones Questionnaire
8	NIH Toolbox - Global
8	NIH Toolbox - Global
9	BSFQ
9	Before-School Functioning Questionnaire
10	MBPC
10	Memory and Behavior Problems Checklist
11	EASI
11	Elder Abuse Suspicion Index
12	NIH Toolbox Sensation and Pain Battery
12	NIH Toolbox Sensation and Pain Battery
13	WRB-S

13	Weekly Record of Behavior - short form
14	WRB
14	Weekly Record of Behavior
15	CANTAB-AL
15	Cambridge Neuropsychological Test Automated Battery for Abuse liability
16	JADAS-71
16	Juvenile Arthritis Disease Activity Score
17	ATLAS
17	Age, Treatment with systemic antibiotics, Leukocyte count, serum Albumin and Serum creatinine
18	RLS-DI
18	Restless Legs Syndrome-Diagnostic Index
19	SPES
19	SCOPA
19	Scales for Outcomes in Parkinson’s Disease - Motor function
20	SOS-SAH
20	Questionnaire for the Screening of Symptoms in aneurysmal Subarachnoid Hemorrhage
21	KSPT
21	Kaufman Speech Praxis Test
22	Movement ABC-2
22	Movement Assessment Battery for Children - Second Edition
23	BODE index
23	Body-Mass Index, Airflow Obstruction, Dyspnea, and Exercise Capacity Index
24	ODSS
24	Overall Disability Sum Score
25	SDAI
25	Simple Disease Activity Index
26	PDMS-2
26	Peabody Developmental Motor Scales - Second Edition
27	SCORAD
27	Scoring in Atopic Dermatitis
28	C-ACT

28	Childhood Asthma Control Test
29	PREFIT Battery
29	Field-based FITness testing in PREschool children
30	GELP Score
30	GELP Score
31	RECAP-V1
31	Remote COVID-19 Assessment in Primary Care
32	Predictive Model to Determine the Level of Care in Patients Confirmed with COVID-19
32	Predictive Model to Determine the Level of Care in Patients Confirmed with COVID-19
33	GTI 2.0
33	Glucorticoid Toxicity Index 2.0
34	CKRS
34	Cincinnati Knee Rating System
35	MSEL
35	Mullen Scales of Early Learning
36	DAI - UCDAI
36	Disease Activity Index - Ulcerative Colitis Disease Activity Index
37	Valent and Modified Valent Response Criteria
37	Valent and Modified Valent Response Criteria
38	4C Deterioration Model
38	Coronavirus Clinical Characterisation Consortium Deterioration Model
39	CSBSS for Diagnostic Evaluation of COVID-19 Patients
39	Clinical Symptom-based Scoring System for Diagnostic Evaluation of COVID-19 Patients
40	ACHS
40	Assessment of Children's Hand Skills
41	WFH Hemophilia Physical Examination Score (Gilbert Score)
41	World Federation of Hemophilia Physical Examination Score (Gilbert Score)
42	NIMH-LCM
42	National Institute of Mental Health-Life-Chart Method
43	SRI
43	SLE Responder Index

44	NIH Consensus Criteria in cGVHD
44	National Institutes of Health Consensus Criteria in Chronic Graft-versus-Host Disease
45	ACR-N
45	American College of Rheumatology N
46	MWC PEDI-CAT
46	Manual Wheelchair Short Scale Pediatric Evaluation of Disability Inventory-Computer-Adaptive Tests
47	NEWS2
47	National Early Warning Score
48	HINT
48	Harris Infant Neuromotor Test
49	TOCS
49	Test of Childhood Stuttering
50	SCoRS
50	Schizophrenia Cognition Rating Scale
51	PPQSA
51	Partner-Patient Questionnaire for Shared Activities
52	UDysRS
52	Unified Dyskinesia Rating Scale
53	W-QLI
53	Wisconsin Quality of Life Index
54	LANSS
54	Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale
55	TEAQV
55	Tableau d'Evaluation Assistée de la Qualité de Vie
56	MPQOL
56	The Miami Pediatric Quality of Life Questionnaire: Parent Scale
57	COHQoL
57	Child Oral Health Quality of Life Questionnaire
58	Family System Test
59	CDR
59	Clinical Dementia Rating

60	PSQI
60	Pittsburgh Sleep Quality Index
61	SDI
61	Social Dysfunction Index
62	CHIP
62	Child Health and Illness Profile
63	PSYCHLOPS
63	Psychological Outcome Profiles
64	ODEON
64	Objectif Douleur En Ophtalmologie et Neuro-ophtalmologie
65	C-SSRS
65	Columbia-Suicide Severity Rating Scale
66	ADAS-COG
66	Alzheimer's Disease Assessment Scale, Cognitive part
67	SE-ADL
67	Schwab and England Activities of Daily Living scale
68	ACSS
68	Asthma Control Scoring System
69	PEDI
69	Pediatric Evaluation of Disability Inventory
70	ASI
70	Addiction Severity Index
71	ASFQ
71	Antipsychotics and Sexual Functioning Questionnaire
72	SLICC/ACR damage index
72	SLICC damage index
72	ACR damage index
72	Systemic Lupus International Coordinating Committee American College of Rheumatology Damage Index
73	CDAI
73	Crohn's Disease Activity Index
74	SLEDAI-2K 10 days

74	Systemic Lupus Erythematosus Disease Activity Index 2000 10 days
75	Bayley III
75	Bayley Scales of Infant and Toddler Development, Third Edition
76	SLAM
76	Systemic Lupus Activity Measure
77	PCDAI
77	Pediatric Crohn Disease Activity Index
78	Vesikari Clinical Severity Scoring System
79	PedsQL Family Impact Module
79	Pediatric Quality of Life Inventory Family Impact Module
80	UPDRS
80	Unified Parkinson’s Disease Rating Scale
81	ASAS HI
81	Assessment of SpondyloArthritis International Society Health Index
82	FARS
82	Friedreich's Ataxia Rating Scale
83	B&B Scale
83	Biberoglu and Behrman Scale
84	Cairo-Bishop criteria
84	Cairo-Bishop criteria
85	ASI – 5th Edition Clinical Training Version
85	Addiction Severity Index – 5th Edition Clinical Training Version
86	ASI-Lite-CF
86	Addiction Severity Index Lite-CF
87	ASI - Lite: Clinical Trials Network Version – Part 1
87	Addiction Severity Index – Lite: Clinical Trials Network Version – Part 1
88	ASI - Lite: Clinical Trials Network Version – Part 2
88	Addiction Severity Index – Lite: Clinical Trials Network Version – Part 2
89	BP-CoRS
89	Bipolar Cognition Rating Scale
90	SEMI

90	Subjective Experience of Medication Interview
91	PSYCHLOPS Kids
91	Psychological Outcome Profiles for Kids
92	BCRSS
92	Brescia-Covid Respiratory Severity Scale
93	WOB
93	Work of Breathing Scale
94	COVID-GRAM
94	COVID-GRAM Critical Illness Risk Score
95	SOAPP-8
95	Screener and Opioid Assessment for Patients with Pain – 8 items
96	COMM-9
96	Current Opioid Misuse Measure - 9 items
97	DBS-CG
97	Dementia Burden Scale-Caregiver
98	CMS
98	Constant-Murley Score
99	MNSI
99	Michigan Neuropathy Screening Instrument
100	OARS
100	Older Americans Resources and Services Multidimensional Functional Assessment Questionnaire
101	SCORMA
101	SCORing MAstocytosis Index
102	MD-CRS (4-18)
102	Movement Disorder - Childhood Rating Scale (4-18 yrs)
103	SIBAT
103	Suicide Ideation and Behavior Assessment Tool
104	MD-CRS R (4-18)
104	Movement Disorder - Childhood Rating Scale Revised (4-18 yrs)
105	PACA
105	Palliative Care Assessment

106	PHQ
106	Patient Health Questionnaire
107	MD-CRS (0-3)
107	Movement Disorder - Childhood Rating Scale (0-3 yrs)
108	SLEDAI
108	Systemic Lupus Erythematosus Disease Activity Index
109	SLEDAI-2K SRI-50
109	Systemic Lupus Erythematosus Disease Activity Index 2000 Responder Index 50
110	BARC
110	Bleeding Academic Research Consortium Scale
111	QLQ-IR
111	QLQ-SR
111	Oregon Quality of Life Questionnaire Interviewer Rating version
111	Respondent Self-Report version
112	MDHAQ
112	MultiDimensional Health Assessment Questionnaire
113	SLEDAI-2K 30 days
113	Systemic Lupus Erythematosus Disease Activity Index 2000 30 days
114	JADAS-27
114	Juvenile Arthritis Disease Activity Score
115	POSAS
115	Patient and Observer Scar Assessment Scale
116	RSAT
116	Rothschild Scale for Antidepressant Tachyphylaxis
117	JADAS-10
117	Juvenile Arthritis Disease Activity Score
118	UMSARS
118	Unified Multiple System Atrophy Rating Scale
119	JIA DOI
119	Juvenile Idiopathic Arthritis Definition of Improvement
120	MMDAI

120	Modified Mayo Disease Activity Index
121	OPDREC
121	Objective Primary Disease Response Evaluation Criteria
122	KSADS-COMP - Clinician administered
122	Kiddie Schedule for Affective Disorders and Schizophrenia - Computerized versions - Clinician administered
123	CADSS-1
123	Clinician-Administered Dissociative States Scale
124	ESSDAI
124	European League Against Rheumatism (EULAR) Sjögren Syndrome Disease Activity Index
125	AIHQ
125	Ambiguous Intentions Hostility Questionnaire
126	Mayo
126	Mayo Score
127	DSM-IV
127	Diagnostic and Statistical Manual of Mental Disorders, 4th edition
128	NAPPA
128	Nail Assessment in Psoriasis and Psoriatic Arthritis
129	IBD-DI
129	Inflammatory Bowel Disease - Disability Index
130	PFDI-46
130	Pelvic Floor Distress Inventory-46
131	CARATKids
131	Control of Allergic Rhinitis and Asthma Test for children
132	UNC DEMS
132	University of North Carolina Dry Eye Management Scale
133	COWS
133	Clinical Opiate Withdrawal Scale
134	CVS-Q
134	Computer Vision Syndrome Questionnaire
135	Work Ability Index
135	WAI

136	WHI
136	Work and Health Interview
137	WPI
137	Work and Productivity Index
138	GFS
138	General Function Score
139	Villalta scale
140	BHVI scale (CCLRU)
140	Brien Holden Vision Institute scale (Cornea and Contact Lens Research Unit grading scale)
141	PSFS 2.0
141	Patient Specific Functional Scale 2.0
142	ProFitMap-neck
142	Profile Fitness Mapping neck questionnaire
143	KS
143	Knee Society Clinical Scoring System
144	KSS
144	Knee Society Score
145	mNIS+7
145	modified Neuropathy Impairment Score +7
146	NIS+7
146	Neuropathy Impairment Score+7
147	PSYCHLOPS Teen
147	Psychological Outcome Profiles for Teenagers
148	PostopQRS
148	Post-operative Quality Recovery Scale
149	RMI
149	Rivermead Mobility Index
150	PDAQ-15
150	Penn Parkinson's Daily Activities Questionnaire-15
151	PUFI
151	Prosthetic Upper Extremity Functional Index

152	RHS
152	Revised Hammersmith Scale
153	PEDI-CAT
153	Pediatric Evaluation of Disability Inventory Computer-Adaptive Tests
154	Nutri-CoV Score
154	Nutricion Covid-19 Score
155	Bayley-4
155	Bayley Scales of Infant and Toddler Development, Fourth Edition
156	CTP
156	Child-Turcotte-Pugh Score
157	COVID-AID risk tool
157	COVID-19 Admission to Death risk tool
158	qCSI
158	Quick COVID-19 Severity Index
159	4C Mortality Score
159	Coronavirus Clinical Characterisation Consortium Mortality Score
160	CIAAD
160	COVID-19 Infectious Acute Abdomen Distinguishment
161	Revised Response Criteria for Malignant Lymphoma
161	Revised Response Criteria for Malignant Lymphoma
162	SSI
162	Stuttering Severity Instrument
163	FTM
163	Fahn-Tolosa-Marin Clinical Rating Scale for Tremor
164	AKUSSI
164	Alkaptonuria Severity Score Index
165	IBHQ
165	Impact of Bronchiolitis Hospitalisation Questionnaire
166	CoV19-OM ICU Score
166	CoV19-OM Intensive Care Unit Score
167	SELENA-SLEDAI

167	Systemic Lupus Erythematosus Disease Activity Index
168	Reponse Assessment for Waldenström Macroglobulinae
168	Reponse Assessment for Waldenström Macroglobulinaemia
169	ACQ
169	Asthma Control Questionnaire
170	Revised Response Criteria for Malignant Lymphoma
170	Revised Response Criteria for Malignant Lymphoma
171	DAS
171	DAS-28 ESR
171	Disease Activity Score - Erythrocyte Sedimentation Rate
172	ACR20
172	ACR50
172	ACR70
172	American College of Rheumatology
173	CDAI
173	Clinical Disease Activity Index
174	DAS
174	DAS-28 CRP
174	Disease Activity Score - C-Reactive Protein
175	PsARC
175	Psoriatic Arthritis Response Criteria
176	JIA
176	Pediatric ACR30
176	Pediatric ACR50
176	Pediatric ACR70
176	Pediatric American College of Rheumatology criteria
177	LDI
177	DSS
177	Leeds Dactylitis Index
177	Dactylitis Score Sheet
178	CELF

Appendix 4.4: Use of PROMs and composite measures in phase IV trials' outcomes

Appendix 4. Use of PROMs and composite measures in phase IV trials' outcomes

	Number of outcomes reporting instrument (%)		Number of outcomes
	PROMs	Composite measures	
Outcomes utilising at least one instrument	12,837 (8.05)	2,146 (1.35)	159,386
Outcome type			
Primary	2,723 (6.31)	523 (1.21)	43,150*
Secondary	9,649 (8.82)	1543 (1.41)	109,410
Other	465 (6.81)	79 (1.16)	6,826

*5,791 trials reported multiple primary outcomes

Appendix 4.5: Use of PROMs and composite measures in phase IV trials over time

Appendix 5. Use of PROMs and composite measures in phase IV trials' outcomes

	Number of trials reporting instrument (%)		Number of trials
	PROMs	Composite measures	
Year (First Posted Date)			
1999	4 (30.77)	1 (7.69)	13
2000	4 (80)	1 (20)	5
2001	0 (0)	0 (0)	11
2002	7 (25.93)	0 (0)	27
2003	7 (15.91)	2 (4.55)	44
2004	14 (25.45)	1 (1.82)	55
2005	368 (21.92)	46 (2.74)	1,679
2006	259 (19.71)	31 (2.36)	1,314
2007	298 (20.97)	52 (3.66)	1,421
2008	409 (20.82)	67 (3.41)	1,964
2009	296 (17.75)	59 (3.54)	1,668
2010	320 (19.74)	75 (4.63)	1,621
2011	306 (19.08)	52 (3.24)	1,604
2012	343 (20.51)	62 (3.71)	1,672
2013	336 (19.29)	74 (4.25)	1,742
2014	371 (19.62)	74 (3.91)	1,891
2015	390 (19.42)	62 (3.09)	2,008
2016	405 (20.87)	87 (4.48)	1,941
2017	346 (20.07)	67 (3.89)	1,724
2018	330 (21.32)	67 (4.33)	1,548
2019	374 (24.52)	84 (5.51)	1,525
2020	390 (24.7)	89 (5.64)	1,579
2021	219 (25.64)	49 (5.74)	854
N/A	16 (24.24)	3 (4.55)	66

Appendix 4.6: The 30 most frequently used composite measures

Appendix 6. The 30 most frequently used composite measures

Measure	Number of trials	%
Pittsburgh Sleep Quality Index	117	0.42%
Bleeding Academic Research Consortium Scale	105	0.38%
American College of Rheumatology	80	0.29%
Diagnostic and Statistical Manual of Mental Disorders, 4th edition	75	0.27%
Unified Parkinson's Disease Rating Scale	66	0.24%
Disease Activity Score - Erythrocyte Sedimentation Rate	61	0.22%
Asthma Control Questionnaire	51	0.18%
Clinical Disease Activity Index	51	0.18%
Mayo Score	48	0.17%
Patient Health Questionnaire	47	0.17%
Columbia-Suicide Severity Rating Scale	46	0.16%
Stuttering Severity Instrument	43	0.15%
Knee Society Score	40	0.14%
Simple Disease Activity Index	38	0.14%
Crohn's Disease Activity Index	38	0.14%
Alzheimer's Disease Assessment Scale, Cognitive part	36	0.13%
Elder Abuse Suspicion Index	34	0.12%
Systemic Lupus Erythematosus Disease Activity Index	23	0.08%
Scoring in Atopic Dermatitis	20	0.07%
Clinical Dementia Rating	19	0.07%
Modified Medical Research Council Dyspnea Scale	18	0.06%
Patient and Observer Scar Assessment Scale	14	0.05%
Child Health and Illness Profile	12	0.04%
Addiction Severity Index	11	0.04%
Constant-Murley Score	11	0.04%
Systemic Lupus Erythematosus Disease Activity Index	11	0.04%
Bayley Scales of Infant and Toddler Development, Third Edition	10	0.04%
Clinical Opiate Withdrawal Scale	10	0.04%
Movement Disorder Society-sponsored revision of the Unified Parkinson's Disease Rating Scale	9	0.03%
Pediatric Crohn Disease Activity Index	9	0.03%

Appendix 4.7: Overview of instruments mentioned in the manuscript

Appendix 7. Overview of instruments mentioned in the manuscript

Based on the PROQOLID descriptions

Patient-reported Outcome Measures

- SF-36 Health Survey

The SF-36 was developed during the Medical Outcomes Study (MOS) to measure generic health concepts relevant across age, disease, and treatment groups. The SF-36 is the most frequently used PRO instrument in clinical trials today. Therapeutic area: Generic

- EQ-5D

To assess health outcome from a wide variety of interventions on a common scale, for purposes of evaluation, allocation and monitoring. Therapeutic area: Generic

- Montgomery-Asberg Depression Rating Scale

To detect change in trial of antidepressant medicines. Therapeutic area: Behavior and Behavior Mechanisms

- Western Ontario and McMaster Universities Arthritis Index

To assess osteoarthritis-related disability in the hip and/or knee. Therapeutic area: Musculoskeletal Diseases

- Brief Pain Inventory

To assess the severity of pain and the impact of pain on daily functions. Therapeutic area: Musculoskeletal and Neural Physiological Phenomena, Pathological Conditions, Signs and Symptoms, Psychological Phenomena

- Health Assessment Questionnaire

To assess the difficulty in performing activities of daily living. The HAQ was originally designed for adult arthritics, it has since been used in a wide range of research settings. Therapeutic area: Generic, Musculoskeletal Diseases

- Hospital Anxiety and Depression Scale

To detect states of anxiety and depression. Therapeutic area: Behavior and Behavior Mechanisms, Mental Disorders

- SF-12 Health Survey

Developed to be a much shorter, yet valid, alternative to the SF-36® for use in large surveys of general and specific populations as well as large longitudinal studies of health outcomes. Therapeutic area: Generic

- Dermatology Life Quality Index

To measure the Quality of Life of dermatology patients and to be used as an outcome measure in health services research. Therapeutic area: Skin and Connective Tissue Diseases

- Life Quality Index

The LQI is a self-administered questionnaire developed specifically for patients/family members involved in intravenous immunoglobulin (IVIG) treatments to assess patients' perceptions of their quality of life. The 15 items are divided into four domains: treatment interferences (6 items), therapy-related problems (4 items), therapy setting (3 items) and treatment costs (2 items). Items are rated on a 7-point Likert-type scale ranging from 1: "Extremely bad" to 7: "Extremely good". Total score range for 15 to 105 with higher score

indicating the highest possible satisfaction with factors such as independence, therapy convenience, social/school/work activities, and health and travel costs.

- Epworth Sleepiness Scale

To measure a subject's usual level of daytime sleepiness or average sleep propensity. Therapeutic area:

Pathological Conditions, Signs and Symptoms

- Asthma Control Test

To assess asthma control. Therapeutic area: Immune System Diseases, Respiratory Tract Diseases

- Pain Catastrophizing Scale

To assess the state of mind of patients in pain through a comprehensive evaluation instrument that encompasses the different perspectives on worrying. Therapeutic area: Generic

- International Index of Erectile Function

To be a brief, reliable, self-administered questionnaire of erectile function in cross cultural settings detecting treatment-related changes in patients. Therapeutic area: Male Urogenital Diseases, Mental Disorders

- COPD Assessment Test

To measure the health status of patients with COPD. Therapeutic area: Pathological Conditions, Signs and Symptoms, Respiratory Tract Diseases

- Oswestry Disability Index

To indicate the extent to which a person’s functional level is restricted by disability. Therapeutic area:

Nervous System Diseases, Pathological Conditions, Signs and Symptoms, Rare disease (Orphanet definition), Wounds and Injuries

- Balanced Inventory for Spinal disorders

To assess the impact of back end leg pain on well-defined physical, social and mental aspects, and on the quality of life. Therapeutic area: Musculoskeletal Diseases

- International Prostate Symptom Score

To capture the severity of urinary symptoms related to benign prostatic hyperplasia. Therapeutic area: Male Urogenital Diseases

- Quality of Life Scale

To assess quality of life for chronic illness populations. It is also valid for healthy populations. Therapeutic area: Generic

- Ocular Surface Disease Index

To provide a rapid assessment of the range of ocular surface symptoms, including symptoms related to chronic dry eye, their severity, and their impact on the patient’s ability to function. Therapeutic area: Eye Diseases

- Severity of Dependence Scale

To evaluate the severity of psychological dependence on different types of drugs. Therapeutic area: Chemically-Induced Disorders, Mental Disorders

- Knee Injury and Osteoarthritis Outcome Score

To assess Knee Injury and Osteoarthritis. Therapeutic area: Musculoskeletal Diseases, Wounds and Injuries

- Sheehan Disability Scale

To assess functional disability in work, social, and family life. Therapeutic area: Mental Disorders

- Beck Depression Inventory - Second Edition

To measure the severity of depression in adults and adolescents. Therapeutic area: Behavior and Behavior Mechanisms

- Kansas City Cardiomyopathy Questionnaire

To provide a better description of health related quality of life in patients with Congestive Heart Failure (CHF). Therapeutic area: Cardiovascular Diseases

- Total Symptom Score

Total Symptom Score is the sum of 4 symptoms reported in Rhinitis symptoms: runny nose, itchy nose, sneezing, and ocular pruritus rated on a categorical severity scale of 0 to 3 [0=none; 1=mild; 2=moderate; 3 =severe]. The maximum score is 12.

- St George’s Respiratory Questionnaire

To assess health in chronic airflow limitation. Therapeutic area: Immune System Diseases, Pathological Conditions, Signs and Symptoms, Rare disease (Orphanet definition), Respiratory Tract Diseases

- Patient Health Questionnaire

To diagnose mental disorders in primary care. Therapeutic area: Behavior and Behavior Mechanisms, Mental Disorders

- Total Nasal Symptom Score

To assess rhinitis symptoms. Therapeutic area: Immune System Diseases, Otorhinolaryngologic Diseases, Respiratory Tract Diseases

Composite Measures

- Pittsburgh Sleep Quality Index

To provide a reliable, valid, and standardized measure of sleep quality - To discriminate between "good" and "poor" sleepers - To provide an index that is easy for subjects to use and for clinicians and researchers to interpret - To provide a brief, clinically useful assessment of a variety of sleep disturbances that might affect sleep quality. Therapeutic area: Mental Disorders, Nervous System Diseases

- Bleeding Academic Research Consortium Scale

To propose a new objective, hierarchically graded, consensus classification for bleeding. Therapeutic area: Cardiovascular Diseases

- American College of Rheumatology

To measure disease activity in rheumatoid arthritis (RA) clinical trials. Therapeutic area: Immune System Diseases, Musculoskeletal Diseases, Skin and Connective Tissue Diseases

- Diagnostic and Statistical Manual of Mental Disorders

Psychiatric Diagnoses are categorized by the Diagnostic and Statistical Manual of Mental Disorders, 4th. Edition. Better known as the DSM-IV, the manual is published by the American Psychiatric Association and covers all mental health disorders for both children and adults. It also lists known causes of these disorders, statistics in terms of gender, age

at onset, and prognosis as well as some research concerning the optimal treatment approaches.

- Unified Parkinson’s Disease Rating Scale

To measure the severity of symptoms and signs of Parkinson's Disease. Therapeutic area: Nervous System Diseases

Appendix 5.1: Patient experts' interview topic guide

Appendix 1. Patient experts interview topic guide.

Introduction:

Introduce self as a UoB PhD student and that this interview is being undertaken as part of the research project funded by unrestricted educational research grant from GSK.

Study recap (general purpose of the interview):

Patient-reported outcomes (PROs) represent health status as reported directly by the patient, without interpretation by a clinician or anyone else. PROs are often collected in trials to understand the impact of disease and treatment on patient symptoms and quality of life. They can be used to help assess if a treatment is safe and tolerable. Once drugs have been tested in trials and approved by regulators for use we still want to know about how effective the therapy is, and if it is safe as it is used in the broader target population. This is called real-world evidence (RWE).

PROs are usually collected via questionnaires that elicit information about symptoms, physical functioning and/or health-related quality of life. The objective of this study is to better understand the use of this type of health questionnaires in the long-term studies of drugs following the completion of clinical trials. Today, we would like to find out more about your views about collecting this information in routine medical practice to assess if a treatment that have been approved for use are working as expected.

Health questionnaires can be completed directly or remotely, using paper, mobile apps, telephone or being asked by health care staff and recorded in patients' health records.

Consent

Check that the respondents are still happy to take part and have signed the consent form. Participants will be reminded that all individual self-identifiers will be removed before transcripts are analysed and that they can stop the interview at any time.

Background information:

- Have you ever been asked to complete a questionnaire about your health? Where? What kind of questions were they?
  Prompts: Did you provide that information? Was it in a clinical trial? Have you ever been asked to complete health questionnaire in routine clinical care? If so, in what clinical setting? Have any steps been taken to encourage you to complete health questionnaire*? Have you been informed how this information can be used to manage your care?*

Main questions:

1) Would you be willing to complete health questionnaires to provide evidence on risks and benefits associated with treatment?
   Prompts: Do you think other patients would be?

2) What would make you more likely to complete health questionnaires as part of your process of care?
   Prompt: Would you expect this information to be seen by your doctor and would this impact on your decision to complete?

3) How often will you be willing to complete a health questionnaire? Would you be willing to use your own smartphone/computer to report PRO data?
   Prompt: Could you see challenges with this? Thinking about your friends and family would they be willing to do this – do your foresee any challenges for them or other broader members of society?

4) How much time are you willing to spend on filling the questionnaire?
   Prompt: Are you willing to complete longer questionnaires if you feel questions are important to you?

5) Would you like to receive reminders to complete questionnaire?

6) Do you have any concerns about providing PROs as part of your routine care?

7) Do you mind if pharmaceutical company would use your anonymised responses to test effectiveness of their products?

8) In what ways do you think medical teams can use the results of these questionnaires?
   Prompts: How well does it fit with how care is delivered now? What are likely issues or complications that may arise?

9) What things would we need to consider in collecting this information?
   Prompt: whether it will inform their care, patient burden, relevance of questions to the patient

10) Would you need support with providing PRO data? What kind of support?
    Prompt: What support might other patients need?

11) Have you ever been involved in co-designing long term studies to ensure that drugs that have been approved for use are working as expected? Have you ever been involved in selecting a health questionnaire to be used in a study? What aspects should be considered when selecting it?

12) Do you think there is a need for patients to be given some training about the importance and how to complete these questionnaires? Are you aware of any training, resources or other forms of support to inform patients about PROs? How this could be improved?
Prompt: If aware of the education campaigns are there more or less visible than campaigns targeting other problems?

13) Do you have anything else to add?

Appendix 5.2: Other experts' interview topic guide

Appendix 2. Other experts interview topic guide.

Introduction:

Introduce self as a UoB PhD student and that this interview is being undertaken as part of the research project funded by unrestricted educational research grant from GSK.

Study recap (general purpose of the interview):

Real-world evidence studies are used to assess the long-term effectiveness and safety of health interventions. Patient-reported outcomes could play an important role in this evidence base describing the impact of healthcare interventions on quality of life, daily activities and symptoms. Today, I would like to find out more about your perspective on current and future PRO use for RWE generation. The objective of this study is to better understand how different aspects related to PRO data collection, analysis and use should be approached to maximise the potential benefits of implementing PROs for RWE generation. I would also like to explore potential challenges to use of PROs in real-world evidence generation. PRO RWE data can be collected directly or remotely through various study designs, using questionnaires, mobile apps, telephone or being captured in patients' health records.

Consent

Check that the respondents are still happy to take part and have signed the consent form. Participants will be reminded that all individual self-identifiers will be removed before transcripts are analysed and that they can stop the interview at any time.

Background information:

- Can I start by asking what your role is?
  How long have you been in the post, what are your key responsibilities?
- Does your role involve collecting, using, or analysing PRO data?
  If yes, what is your involvement? How do you or your organisation use PROs in RWE generation?

Main questions:

1) What do you think the value of using PROs in RWE generation is?
   Prompts: Can you compare it to other types of outcomes? Which areas would benefit the most by greater use of PROs for RWE generation?

2) What are the most important barriers which hold back the full implementation of PRO data for RWE generation?
   Prompt: How these challenges might be addressed? Are infrastructure changes i.e. IT systems, staffing to support PRO usage, adaptions to existing workflow and care delivery systems needed? What about time and money needed? Can legal issues e.g. patient consent, data ownership be obstacles? What about willingness to collect/provide data by staff and patient, Missing baseline information, Missing data points?

3) What would encourage/discourage the use of PROs in RWE studies?
   Prompt: What evidence supports or discourage the use of PROs for RWE generation?

4) Can you describe how the PROs could be integrated into current RWE research/ regulatory process/reimbursement process?
   Prompts: How well does it fit with existing work processes and practices? What are likely issues or complications that may arise? What actions should be undertaken to minimise this burden?

5) What aspects should be considered when selecting PRO instrument to be used for RW study?
   Prompts: Do you expect to see a preference for a particular type of measures e.g. symptom or generic QoL PROs? Who should be involved in this decision-making process?

6) Do you feel that there is sufficient understanding and guidance on how PROs can be optimised in RWE?
   Prompt: In which areas is this lack of guidance most acute (if participant has identified a lack of guidance)? How should this lack of understanding/guidance be addressed?

7) Thinking about your answers so far is there anything additional you would like to add from your organisational perspective?
   Prompts: Is your organisation planning to increase/promote the use of PROs in RWE generation?

8) Do you have anything else to add?

Other question if time allows

<u>Data collection</u>

Is primary or secondary use of PRO data for RWE generation more appropriate? Are there any specific considerations that should be given to the mode of PRO data collection?

Prompts: How these can be addressed?

Should any special considerations be given about PRO data collection among underserved patient groups/ patients from diverse backgrounds?

Data analysis

Is a special approach for analysis of PRO data needed to enable RWE generation for regulatory, reimbursement or health policy?

Prompts: Risk-adjustment for patient characteristics, pooling data across multiple health systems, missing data (single data point vs. multiple data points).

Uptake of PROs

What kind of data quality requirements, policies, regulations, or guidelines can influence the decision to uptake PROs in RW studies?

Prompt: At what level could it be introduced (local, state, national, international)?

Who are the key influential stakeholders for the wider implementation of PROs for RWE generation?

Prompt: What could be an efficient engagement strategy to get these people/organisations on board?

Resources

Do you have sufficient resources to implement PROs for RWE generation? What costs need to be incurred to implement them?

Prompts: Who should be covering costs associated with PRO data collection for the purpose of RW study?

Education & training

Are you aware of any training, resources or other forms of support to help with PROs implementation? How this could be improved?

Are you encouraged to network with colleagues outside your setting?

Appendix 5.3: Summary of key findings – CFIR domains, belief statements and representative quotes.

Appendix 3. Summary of key findings – CFIR domains, belief statements and representative quotes.

CFIR constructs	Themes/inner settings/individuals	Emergent issues	Illustrative quotation
I. Innovation domain			
Innovation Evidence-Base The degree to which the innovation has robust evidence supporting its effectiveness	Consultation duration	The use of PROs in routine practice does not prolong consultation time	#1: "Whether it prolongs the consultations and although I have data showing these things (PROs) don't prolong consultations, that's still the highest concern." R2
	Clinicians' reporting	Health Care Professionals' (HCPs') reporting misses some of the aspects which are important to the patients	#2: "If you just think about side effects, safety and tolerability from the patient perspective, there is so much literature that shows that physicians, doctors, and nurse practitioners are missing a lot of the picture (…) when they report." R30
	Patient management	PROs help to deliver care which is appropriate to the patient's needs	#3: "There were some signals around management. (..) The management improved. There were more appropriate referrals to other specialists." R99
	Willingness to provide data	Patients are generally willing to complete PRO questionnaires	#4: "There's (…) evidence to suggest that patients are willing to provide these data, if they're going to be used." R77
	Health outcomes	The use of PROs in routine care leads to better outcomes	#5: "I know studies that support its use in patient care, with (…) benefits for symptom control, for communication, survival..." R2
	Cost containment	The use of PROs in routine care generates savings	#6: "I've seen so many studies (…) where they're like: look how much money I saved." R75
Innovation Relative Advantage The degree to which the innovation is better than other available innovations or current practice	General value statements	High potential of PROs collected in real-world across the entire healthcare decision-making	#7: "Depending on your perspective, there're tons of potentials." R12
		PROs should not be overstated	#8: "It's important to have a balanced concept about the usefulness of PROs. Because it's important not to overstate their value, I think there are a lot of issues methodologically with them, that are still not completely well understood." R100
		Lack of trust in non-clinical, non-randomised trials	#9: "I've actually stayed away from RWE type studies on the basis that I don't understand, and I don't have the confidence with data. (…) I always questioned use of that data because it is such a mess." R74

	Applicability of PROs collected in real-world studies	Safety/tolerability monitoring	#10: “Certainly, one of the key areas is around tolerability. (…) In most clinical trials, (…) before marketing authorization we get good data on efficacy signals and (…) most clinical trials are powered for efficacy, (…) they're virtually never powered for the safety.” R85
		Can inform the individual care of a patient who provided PRO responses	#11: “You collect these PROs to then inform your clinic visit with the physician. (…) The physician is going to have it pop up on the screen before you walk into the room. (…) Oh, your pain is seven, OK, well, we’ve really got to take care of that today.” R30
		RWE informs care by showing real-world effectiveness of health interventions	#12: You could then feedback to clinicians and patients evidence as to (…) what actually happens in the real world, and that would have benefits in terms of clinical decision making, justifying new treatment approaches helping patients understand better what their future looks like.” R12
		Reimbursement decisions	#13: “There is value clearly in having patient-reported outcome measures to inform health technology assessments to better understand patients’ experiences and that data is routinely lacking in real world evidence sources” R80
		Descriptive RWD can inform phase III study set-up	#14: “Real world studies give you that flexibility to tap into some of those questions that you might otherwise overlook if you've jump straight into your phase III RCT.” R35
		Maximizing value of PRO data collection	#15: “If we’re going to be taking the time and investing the resources to collect PRO data we want to maximize its value and use it for as many different ways as we can to advance patient-centered care. (…) To demonstrate (them) to patients, you know they’re spending their time, and to demonstrate to institutions – they’re investing their resources, (that) is producing value.” R77
	Patient centricity	PROs improve communication with patients	#16: “This is really a communication intervention to try to improve symptom control.” R91
		PROs inform about patients' perception of their health	#17: “One added value is the PROs can give you information that you can’t get from other real-world data. Most of our real-world data is based on administrative databases, so we look at electronic medical records synthesised across patients, aggregated, pooled. So, we can see what procedures people get. We can see what doctors, they meet. We can look at how many hospitalizations they have. We can look at discharge diagnoses from those hospitalizations. We can see if they’ve been in the emergency room, etc. But we can’t get the patient's perspective on any of that.” R12

		A helpful self-diagnosis tool for the patients	#18: “It could possibly help them going forward as part of their treatment, (…) and even a self-diagnosis, I suppose.” R18
		PROs help to prioritise and bespoke care according to patients’ needs	#19: “Risk stratification is really important, because it means that the right patient gets the right treatment at the right time in the right location.” R16
		Strengthening the voice of underrepresented populations	#20: “It’s a voice that obviously has been completely underrepresented in the healthcare system, right? (…) PROs are a vehicle to get their information out there.” R75
	Information contained in PROs	PROs can provide a more complete picture on adverse events than from clinical report	#21: “If you look at the data from clinical trials and the adverse event data, you don't get a really complete picture of the adverse events. I mean if it's a grade 3 or 4 you do, of course, get that marking that this is a serious adverse event, but the nice thing with patient experience data, is that, it's being tracked along on a regular basis. You're able to see like: OK somebody reported severe diarrhoea which was then resolved by, because you have follow-up assessments, and so you see it getting resolved, whereas a clinician put in a note to the CRF that the grade three or four diarrhoea.” R30
		Some PROs inform about the impact of treatment on quality of life, which is a broader concept	#22: “We can have (…) kind of clinical binary, did it work or not, did it lower this lab value or not, that type of thing, but in terms of quality of life, is that actually helping the patient?” R83
		PROs has application in symptomatic diseases	#23: “There are some very serious diseases that have almost no symptoms (…) until you get closer to the end stage. Probably PROs are not all that useful there.” R100
		PROs are subjective but give a more complex picture than wearables	#24: “So that's the difference of wearables. People like them because they think that is objective. Count of what you're doing, but there's still a lot of subjectivity to it.” R30
		PROs help to understand some other types of RWD better	#25: “A lot of times, it is difficult for us to understand why a drug has been prescribed. There is no direct link to the indication. It is rare that we have it. (…). Maybe PRO could be helpful in these.” R26
		PROs demonstrate a more complex picture of the individual	#26: “Comparing to the other sources of RWD, so primary, secondary, registries, indeed a different type of outcome we can collect, quality of life gives a more comprehensive picture. Patient experience is what would add to the social data we already have access to. So yes, for us when we work on PRO data is having more outcomes and soft outcomes and having a broader picture.”R26

	RWE vs RCT	Broader populations and larger sample sizes	#27: “Generalise the findings to a broader population. We know that within the clinical trial setting, because of the many inclusion and exclusion criteria, the population is very defined, very small. What you kind of see with PROs or quality of life measures in these studies, it is quite limited to that specific populations.” R26
		Opportunity to collect data which were not captured in trials	#28: “One of the greatest utilities of real world data are to collect information that either can’t be collected in trials, or is deprioritised.” R75
		Informs about real-world effectiveness	#29: “You can do effectiveness studies of clinical drugs in the real world and find out whether they work as well in the real world, as they do in clinical trials. So, effectiveness versus efficacy.” R12
		Cheaper than trials	#30: “So, it's very expensive to collect PROs in clinical trials, that's a costly prospect, so, you know, it's one of the visions, that you could formally run the clinical trial say for five years and collect PROs on the trial and then, after that you could collect them in the real world and extend your effective follow-up” R12
		Provide information about various sub-populations	#31: “That would be better evaluation of a new drug and it will give you better data. Is it replicating the results from the trial, does it give completely different results, how does it work in other populations, #32: etc.? So, I think there is potential benefit in all of this.” R26
		RWE study can be conducted when a trial is not feasible	#33: “You can’t do clinical trials on everything, so we’ve learned a lot about how things work by doing natural experiments, you know, what’s done in one region (…) versus what’s done in the other region …” R12
		Can inform about subtle changes between treatment regimes	#34: “You have the potential to create a lot of outcome data with subtle differences in the way technologies are used. (…) It could be really informative to find out how different patterns of practice result in different outcomes from the patient's perspective.” R12
		Longer follow-up	#35: “The added value I currently envision is the longer follow up. (…) For example, (…) cancer is becoming more and more curable. It means that we end up with cancer survivors” R26
		Multiple sources of heterogeneity in RWD samples	#36: “That’s what makes it valuable in one sense because it’s so heterogeneous, and you’d hope that some sort of signal would arise up above all that noise.” R12

Innovation Complexity The degree to which the innovation is complicated, which may be reflected by its scope and/or the nature and number of connections and steps	RWD definition	Confusion about RWD definition	#37: “But what the hell is real world? I’m still struggling with that definition. What is that?” R74 #38: “So yeah, I'm still not convinced, you can do real-world data studies with PROs to be real-real-world, because many patients will not participate... So, it's still better than a trial in terms of how generalizable it is, but it will never be you know exactly what (real-world is).” R2
		Only data collected as part of routine care	#39: “I think if someone is (…) use a wearable device, allow someone to monitor them and do that as part of a research program that to me is not real-world evidence. (…) That's research. (…) The real-world evidence is taking stuff that happens in the real world, not people that you convinced to wear a wearable device and monitor them and do research on that. That's a very selected subgroup of patients. That's not real world. Real world would be getting Google data or Facebook data to see what happens (…) in unselective people that have no idea that they're participating in a research.” R12 #40: “If you’re selecting PROs specifically to collect real world data I think you’re missing the point that they ought to be used in clinical practice and then used to inform real world evidence (…). Else, all you’re doing is a broad based population research project, which is a different thing, right? (…) That’s not real world anymore. That’s to me broad based research project.” R12 #41: “You still lose patients who don't want to do it - don't want to consent, and I think it is possibly tricky to actually collect that data without patient consent.” R2
		Everything outside of the clinical trial	#42: “It’s everything, but a clinical trial. (…) It’s a very broad definition. I think that is fine, in terms of the purposes of (…) how this can be useful for a multitude of stakeholders.” R8
		Primary vs secondary use of data	#43: “I think what's more important is to be clear on the source of the data, regardless of what you call it. So, regardless of whether it's real-world evidence or not real-world evidence, (…) (for example) you (can) have secondary data, so all of the PRO data (…) were collected for a different reason, for their primary reason and you're doing it for a secondary reason.”R77

	Ethics	Patients need to be sure of the purpose of PRO data collection	#44: “Having the data anonymised and non-traceable is important to patients, (…) because patients have to learn to build trust and there has to be transparency around the use of PROs. (…) They need to be clear that (…) PRO collection isn't going to be used for any purpose other than the purpose that they've agreed to initially.” R21
		Patient consent is not needed for universal data collection in routine practice	#45: “It's routine care, if it's everyone coming through the door, then that is part of your care and you do not need to sign a separate consent form” R91
		Patient consent needed to use their data for research	#46: “If you want to use it for research, you need to ask the ethics board for permission.” R99 #47: “The portal asks for personal information, and then it asks the question of whether the patient will be interested in participating in research, and if so, these data will be collected. So, there's an ethical piece there that is associated with the ethical board in our institution.” R99
		No standards for obtaining patient consent in real world	#48: “How do you consent patients, what do you do to support patients in terms of making a decision (…) if they want to be part of the PRO study or using PRO data and how would that data be used (…) is absolutely essential and understanding the framework for delivering that content is equally really important.” R85
		Privacy issues apply to all types of RWD, patients should be informed of how data will be used	#49: “I don’t know that the PRO data are so different from any other data that would be used, but I do think we need to be clear and transparent with patients about how all of their data may be used or will be used.” R77
		Not using collected data is unethical	#50: “So, I think we have to be really thoughtful about (…) balance between collecting patient experience data and ensuring that we then use that data and we don't waste their time and efforts.” R30
	Data collection	Much messier data is collected in real world	#51: “(It) is a big data set, but it's often not quite clean; it's not like a data set you get in a clinical trial where statisticians go through and data managers.” R2
		No statistical methods will help when data of low quality	#52: “I just really want to emphasize the data fitness perspective. (…) It's not about the number of data points; it's about the quality of the data. (…) So, you could have the best analytics and understand what you want to study, but if the data aren't collected well, you're in trouble.” R75

		Extensive data management is needed	#53: “Patient-reported outcome, meaning they are self-reported, (…) so it's up to the willingness of a specific patient, whether or not to participate. (…) So, it requires a lot of data management.” R26 #54: “Statisticians have the knowledge and how to impute data. How to improve the quality of data, how to account for potential biases or limitations of the data sets, how to set up the sample size, so your findings are reliable, right?” R26
		Multicountry data collection is challenging	#55: “And how do you collect real-world data across 12 countries in a standardised manner? It is impossible. So, it is very difficult. It's not an easy field to work in, I think.” R74
		ePROs increase the quality of collected data	#56: “Although with electronic PROs that's usually OK - the (data is of better)quality and less patients stop halfway and never continue.” R2
		Selection bias due to voluntary data provision	#57: “Your population may not be completely representative because there are certain characteristics of people who may participate in these things that are different from those who choose not to.” R83
	Data analysis	Missing data is the biggest issue	#58: “I think we would have to really think about how (to) approach missing data. Based on the timing of the data collection. So, I think that’s critical” R8
		Describe who is missing	#59: “So, we don’t have those tools (that are) used in the clinical trials. (…) It’s a huge problem. (…) If you could at least describe your entire population and describe from that who you’ve got data on, that’s a start.” R12
		Use appropriate statistical methods	#60: “Depending on what the data (type it) is, (…) ensuring that appropriate statistical techniques are used to analyse the data. So there would be situations where you could have (…) different reporting along those scales, but you could be able to use some type of statistical technique to adjust for that. (…) Always be ensuring that you are using the right tests for the right data.” R83
		Using data for secondary purposes requires more statistical work	#61: “If we want to use (data) for new research questions (…) then we have to be open to doing the behind the scene work that will make them up to the standards we would need.” R8

		Similar problems apply to other types of RWD	#62: “There's all the variability that applies, that I want to emphasise, applies no more to PRO data than it does to other kinds of real-world evidence, such as (…) varying time points, varying modalities of collection, varying circumstances where the data is being compared. (…) But (…) those things (…) apply to real-world evidence overall not specifically to PROs.” R77
		Level of required data robustness depends on future application	#63: “I think that there are different considerations when you look at the collection of PROMs for different purposes. So, If you look at it from the purpose of drug approval, (…) then I think the considerations are very different. And, in many cases, it’s like keeping the considerations as they are kept in a randomized clinical trial, where you want to get your data perfect” R99 #64: “That depends on your application and how important that is; if you’re doing something more descriptive and understanding the population, it might be less important than if you’re trying to use this data to look at the kind of effects. And obviously, then you need to be doing some sort of risk adjustment process. And obviously, these PROs, when they’re not used as outcome data, can also be useful (…) to kind of better balance patient characteristics at the baseline if you do have this information.” R80 #65: “However, we're not going to be analysing it in any kind of comparative way. We're going to be using it as a descriptive to look at trends over time for our patient population.” R35
		Statistical methods already exist and can be drawn upon from clinical trial settings, but there is need to set up standards for communicating results	#66: “There’s obviously a lot of literature on methods around missing data for PROs. I come across a lot of literature on that. It is often in the context of trials, but it does, I think, extends quite naturally.” R80 #67: “Statisticians (…) can bring it easily from a methodological point of view; they can bring it to the RWD. It's just if you want to convey the added value of PROs you need to have a standard way of communicating results.” R26

	PRO methodology	Measurement situation impacts PRO results	#68: “There are a lot of issues methodologically with them, that are still not completely well understood, which is surprising. (…) The situation is the most important variable in measurement, right? So, when you think about the psychological situation (…) (you need to think) about the motivation of the subject, are they at all motivated by social desirability or are they motivated by the desire to malinger or, you know, not give a true answer exactly. So, that really needs to be considered, because PROs, they're not like biomarkers. (…) They can be measured with a lack of reliability.” R100
		It is not always feasible to use PRO due to the nature of the illness	#69: “I work in a lot with rare diseases and oftentimes, I cannot use a PRO. So, I'm actually more dependent (…) on a caregiver” R8
		The recall period can be problematic when collecting data in real world	#70: “There are some challenges, depending on recall periods and things like this, so if I ask you about your pain and ask you to recall the seven days, this is pretty different to asking you about your pain today.” R30
	RWE infancy	Significant barriers stopping PROs implementation	#71: “If it were easy, we would have done it a long time ago. And stopping dead and it's not been done, because of the tremendous importance of the barriers” R12
		Still challenging to assess the importance of PROs to RWE	#72: “I think we're still really early, and so I don't know that it has a value at this very moment which frustrates me” R30
		Although PROs are successfully used in RCTs, it a new concept in the RWE space	#73: “PROs these days have proven their point. You can see them as a secondary objective in clinical trials; they are knocking on the door of the RWD.” R26
	Barrier types	Operational and methodological barriers	#74: “I think probably most of the barriers are on the operational side. I mean there are methodological challenges which we can get onto, but I think it's more about embedding the kind of a consistent use of PROMs within data collections.” R80
		Secondary PRO data use is hindered due to limited data capture in routine care	#75: “Barriers to measuring PROs in practice (…) are upstream from the barriers to using them in the real world, a lot of them.” R12 #76: “I think it's mainly data collection issues that might be the barriers.” R26
	PRO instruments	Multiple instruments used to measure similar concepts	#77: “When the PRO data are there, there’s the challenge that different measures are being used to assess the same thing and we have limited, although increasing ability to crosswalk scores among different measures.” R77

Innovation Cost The degree to which the innovation purchase and operating costs are affordable	PRO data collection as part of routine care	Expensive system-level implementation projects	#78: “I think the biggest challenge is going to be introducing real-world data collection into the routine practice. (…) Because there isn't the funding for that unless somebody's going to go behind it, like a pharmaceutical company.” R35
		Resource-intensive data collection	#79: “I think it’s very resource intensive, timewise and if I see how PROs questionnaires how they are collected – it’s very resource intensive.” R26
		No need for system-level implementations for some industry sponsored studies	#80: “It (…) depends on kind of study we're talking about. (…) So, if it's like data collected from the electronic health record, then it needs to be in place that they're routinely collecting that data. So, yeah, I would agree for something like that you would need to put in quite a detailed structural change for that department or whatever to be able to routinely (…) collect additional data that they otherwise weren't. So, for that, it would be very challenging. I think for other studies, whereby (…) you're almost setting it up like you do for a clinical trial, where you kind of get the site on board (…), you pay them for their time and collecting the data (…). But of course, you need a big machine there, which is normally the pharmaceutical industry.” R35
		It might not be possible to extrapolate the benefits of close patient monitoring to the system level	#81: “Those studies, while they have really great outcomes, show that they takes a lot of infrastructure and resources to pull that off. I don't know that anybody's like dive into how much the costs would be to scale it to the entire healthcare system.” R30
	Hospital-level cost of data capture	Investments need to align with benefits stemming from the implementation	#82: “There's an upfront cost for that, obviously - and then an ongoing cost and the upfront costs, this is larger because you do need the IT costs, you do need to pay a company to run it, then you potentially start saving afterwards, but it's all predictions, how much you'll save.” R2

II. Outer setting domain			
Critical Incidents The degree to which large-scale and/or unanticipated events disrupt implementation and/or delivery of the innovation	COVID pandemic	COVID distracted healthcare systems from PROs	#83: Especially with COVID, we're trying to keep people alive instead of measuring their PROMs.” R12
		COVID constrained available hospital resources	#84: “It’s more resistance from the hospital IT departments that are busy with COVID and all of us doing the remote work etc.” R2 #85: “There's a nursing staffing shortage in the US right now that has been made much worse by COVID, so we don't even have enough people in the clinic” R91
		COVID impacted patient lives, which is reflected in collected data	#86: “I haven't had GP’s appointment for three years because of COVID.” R3 #87: “Patients have just not been completing their questionnaires because of illness or because they’re not doing their usual activities that they normally do, which then impacts your data because you’re looking at something like activity. You can’t even measure that, because they’re locked down.” R35
Local Attitudes The degree to which sociocultural values (e.g., shared responsibility in helping recipients) and beliefs (e.g., convictions about the worthiness of recipients) encourage the Outer Setting to support implementation and/or delivery of the innovation	How to use PROs for RWE generation	Not enough understanding of how to use PROs in the RWE generation	#88: “No, I do not think there's any understanding.” R85 #89: “I think it's just that there's a lack of consensus within the field on how you would interpret PRO data in the real world setting” R85 #90: “There's no standardised design, how do you standardise the studies, how you standardise the way it's collected.” R74
		Lack of agreement on how to collect data	#91: “I think there’s not necessarily a very visible framework in terms of how you would collect that data. It’s not clear who would fund the collection of that data, so unless it’s a mandated regulatory condition of a marketing authorisation which we do, we can ask companies to collect more data, unless it’s mandatory. Why would you do it, so there has to be an advantage for companies to be able to do it.” R85

		Lack of consensus about types of conclusions which can be supported with RWD	#92: “I don't think there's sufficient robustness in the understanding of exactly how we would use that data going forward for me. What decisions can we make based on that data. These data may be interesting, and it may be providing signals, but what type of follow-up do we need to do, based on that data? R85 #93: “I would say we're probably in the infancy of utilising RWE and RWD (…) in terms of being able to support efficacy. Because we do have a regulatory standard, we have actual law in the US, of what has to be met to be able to make a claim about efficacy.” R8 #94: “Depending on the context of use, there is variation how committees are willing to accept it and the confidence that they have in it. So, if you’re using it for comparison effects, there’s likely to be most scepticism or challenge to it, whereas if you’re using that as more characterisation of a patient group or perhaps like parameterising in an economic model or something, then it might be more accepted.” R80
		For some disease areas, PROs are less important than other types of outcomes	#95: “But for anti-cancer, you’re always going to have survival, progression-free survival, disease-free, all those things are going to be your primary and secondary endpoints. Patient-reported data will always be at the bottom of the endpoint hierarchy or an exploratory, supplementary information.” R30
		PROs are more important outside of comparative effectiveness studies	#96: “But if it’s not (…) effectiveness (…) and it’s more about understanding your patient population, then you have PROs as your primaries and your biological ones can come later.” R35
Local Conditions The degree to which economic, environmental, political, and/or technological conditions enable the Outer Setting to support implementation and/or delivery of the innovation	Collection of PROs in routine care	PROs are still not being routinely collected	#97: “At most venues, PROs are not routinely collected. So, you know, there is a lack of PRO data.” R77
		Lack of necessary infrastructure in place to collect PROs	#98: “But until you have a systematic infrastructure, where you try and collect these data in a systematic way to answer questions, it's just not going to happen opportunistically” R12
	Availability of PROs in RWD repositories	PRO data not available in RWD databases	#99: “These big data curation groups, they don’t have patient-reported outcome data.” R30

Partnerships & Connections The degree to which the Inner Setting is networked with external entities, including referral networks, academic affiliations, and professional organization networks	Collecting data from healthcare providers	Need cooperation form hospital health informatics teams	#100: “We've been begging for about a year, to get the data and then they made a small mistake in it, so we didn't get everything - another six months, and while we got their attention, it took them 10 minutes. But that is kind of how you work with big hospital departments that have other priorities. And home much you pay them, I suppose.” R2
		Data-sharing agreements need to be in place	#101: “Then you need to download the data, so that will get you through the data sharing agreements, all these contractual things.” R2
		Electronic data capture allows for interoperability between different databases	#102: “In that 15 years, every clinic has been gathering more and more data and less and less of it's on paper and more and more of it captured in computing systems. And more we're getting these computer systems to be able to talk together in new ways, and we are going to see an explosion of opportunity and PROs have got to be there.” R40
		The complex process, with the involvement of many stakeholders	#103: “Who downloads the data for you in that RWE (study)? Is it the IT department? So, I think it's a complex procedure and to look at each step of it.” R2
	Networking	Various stakeholders should network across the board	#104: “So I think like regulators, (…), HTAs and other payer societies, (…) professional societies, I think it would be so cool to really advanced space, you need to have some multistakeholder partnerships.(…). And then to also consult patients. So, I think you gotta be broad and kind of aim high, right?” R75 #105: “I think that's why we need to work collectively, proactively, outside of drug development programs to really hone in on how can we best operationalise the collection of this type of data in the real-world setting. In a way, that could be used for those multiple stakeholders.” R8
Policies & Laws The degree to which legislation, regulations, professional group guidelines and recommendations, or accreditation standards support	Existing guidance	Existing guidance can be also applicable (to some extent) to RWE	#106: “I think there’s enough guidance out there. I mean there’s FDA guidance, there’s NICE guidance, so I think there’s enough guidance. It’s actually executing that guidance is the hard part.” R12 #107: “I think there's sufficient, but I think as the field matures that it will advance, so I don't think we're the in a place where we have to say like we don't know enough to do it at all. I think we know enough to do it, I think, over time, will learn how to do it better.” R77

implementation and/or delivery of the innovation		Guidance for PROs in RWE generation is needed across the board	#108: “It comes down to partly around lack of consensus in the sort of requirements for that data collection, say in clinical trials you’ve obviously got (good clinical practice, we don’t have to the same level that sort of a framework for collecting data in the real world setting.” R85 #109: “I mean, even a lot of the guidance which is out there is focused on trials, right? So, we definitely need a better intersection of like epidemiology and PROs.” R75
		Guidance helps the industry to generate meaningful evidence	#110: “When you put up standards and guidance, (…) you give them (industry) the confidence to do things like this, so that you can de-risk it where they can. Of course, ultimately, the evidence has to speak for itself, but let's help them at least try to generate meaningful evidence that is actually interpretable by a decision-maker, right?” R75
	Mandating PRO collection	Universal PRO data collection	#111: “A few years ago, they decided to implement patient-reported outcomes, I think, across all diseases, not just cancer, certainly in cancer across Denmark. All hospital sites became obligatory to start using it, and they are paid.” R2
		Regulators and payers can require data collection for a specific drug or disease	#112: “There are situations where we more directly require data collection, so it is as part of managed access. But in a regulatory context, you obviously have post-marketing surveillance studies and things like that.” R80
		A significant rate of missing data	#113: “Although it’s mandated to collect the PROs on every patient, we only get them in about 60% of patients.” R12
Financing The degree to which funding from external entities (e.g., grants, reimbursement) is available to implement and/or deliver the innovation	Financing PRO data collection	The way of financing highly depends on the goals and objectives of data collection	#114: “Who should pay for it? It depends on what it’s used for.” R80 #115: “You need to make sure that the people who are benefiting from those efficiencies are the ones who are investing the money and collecting the data.” R77 #116: “If people can’t be guaranteed they’re going to be reimbursed for this, it’s not going to happen.” R91
		Alternative cost of data collection	#117: “So, the government de facto is paying for it through the use of taxation. And so, if they spend money on collecting PROs they have less money to spend on something else, so you have to show the value.” R12

		Industry-sponsored prospective data collection	#118: “You're almost setting it up, like you do for a clinical trial, where you kind of get the site on board (and) you pay them for their time and collecting the data.” R35
External Pressure The degree to which external pressures drive implementation and/or delivery of the innovation. Note: Use this construct to capture themes related to External Pressures that are not included in the subconstructs below	Societal pressure	Increasing interest in utilising RWD for decision-making	#119: “I think the field is obviously moving quite quickly now.” R85 #120: “There's a lot of effort in this space right now.” R30 #121: “Obviously, there's been a big boom in the wanting to use real-world evidence to support question marks.” R8
	Market pressure	PROs are being used more widely in routine practice as healthcare providers duplicate workflows of similar facilities	#122: “When one department has used it for some years, then all departments with the same type of patients, they are often asking why we do not use it?” R25
		Regulatory bodies internalise similar regulations	#123: “If you say FDA also does it. (It is) like: Oh, then we also needed it.” R26
	Performance-measurement pressure	Some interest in using PROs for performance measurement, but a lack of benchmarks hinders use	#124: “So, they want to eventually, possibly move to a model where care is judged based on patient perceptions and not on quantity. (…) But we don't have any benchmarks yet. So, we don't know where people should be. So, what percentage of your chemotherapy people should be reporting nausea? Hopefully, it would be low, but we don't know what is low.” R91
III.Inner settings domain			
IT Infrastructure The degree to which technological systems for tele-communication, electronic documentation, and data storage, management, reporting, and analysis support functional performance of the Inner Setting	Healthcare provider	Most healthcare providers have some Electronic Health Records (EHR) system in place and PROs could be integrated there	#125: “I think the IT infrastructure isn't that difficult (…) because (…) most hospitals have electronic records. You can collect patient-reported data using any software, any app and then all you need to do is link it to the electronic records integrated via a standard interface called API.” R2
		EHR system should be able to analyse data instantly and feed back results to the clinician	#126: “In medicine, you want to have somebody come in, fill out the form and have the results available to the physician for that visit, and that requires a certain infrastructure.” R100
		EHR systems have low usability for PRO data collection	#127: “It's a common problem that you buy a new EHR system and the sellers promise everything that you can do anything, including entering PRO, but this is definitely not the case or it is a very primitive way it can handle PRO.” R25

		Data collected as part of prospective studies usually are not fed back to EHRs	#128: “They'll use it for their research purpose, but it doesn't overflow into routine daily clinical care for everyone.” R91
		Multiple prospective studies collect data using different platform	#129: “So (one) organisation (…) develops something for their particular product, and then someone else does something for their particular product and then it is not particularly friendly for health professionals to use.” R41
Work infrastructure The degree to which organization of tasks and responsibilities within and between individuals and teams, and general staffing levels, support functional performance of the Inner Setting		Data collection needs to be integrated into the existing workflows	#130: There's a culture issue and a workflow issue. But both are addressable with effort.” R77
		Implementation is context specific	#131: “So, usually what we have to do is work with each clinic individually. So, even if there were two clinics in the same service line (…), but they were radically different on their workflow.” R91
		PROs compete with other tasks currently in the workflows	#132: “Additions to the process, really will compromise the other processes that are in place. So if, I have to talk to the patient about the PROMs results, I might have no time to talk about the X-rays results, because I have seven minutes visit with the patient.” R99
Compatibility The degree to which the innovation fits with workflows, systems, and processes		PROs are rarely routinely collected at the large scale with integration in the EHR	#133: “Nobody is (collecting PRO data routinely) in the UK in that setting. So basically, they thought it's happening and it's going in the electronic records, well it isn't. There may be one or two places, but it's not going into electronic record.” R2
Funding The degree to which funding is available to implement and deliver the innovation		Data collection is resource intensive	#134: “It needs infrastructure, money, people to be available to collect that data. So, a lot of work needs to be done on this and we are really at the early stages, I think.” R74
		Getting paid by a study sponsor is strictly regulated	#135: “In some countries, you're allowed to pay more, in others, there's quite a lot of restrictions on what you can pay a clinician.” R35
		It is a hospital investment to introduce PRO capture in EHR, so the return on it needs to be seen	#136: “It costs money to implement a system. So you have to have the folks at the top of the hospitals, who make these decisions, believe that this is worth the X thousands to implement a system.” R30

IT infrastructure The degree to which technological systems for tele-communication, electronic documentation, and data storage, management, reporting, and analysis support functional performance of the Inner Setting	Healthcare system	Implementation at the system level is a big infrastructural project, and it is impossible to find private sponsors for that	#137: “To integrate it with the health medical record to make it more useful clinically, that's a big big project and pharma companies not going to pay for that just to get the evidence on the one drug that they want to do the post marketing strategy.” R12
		Fragmented health informatics	#138: “One of the challenges is the fragmented nature of the health system in the sense that every different hospital has different systems in place.” R41
		A common system for data collection by multiple stakeholders would be useful	#139: “If you are a company and you want to collect data in the real-world setting, one of the questions you're going to ask is: well, how much is it going to cost? What systems can I use? Is there already a data capture system that I can plug into to be able to collect that data?” R85
Incentive systems The degree to which tangible and/or intangible incentives and rewards and/or disincentives and punishments support implementation and delivery of the innovation		Using PROs can be beneficial to the entire healthcare system	#140: “If you use clinic-based PRO tools to better manage and personalise the care for patients, you can keep many at home and not bring them into hospital, and you can promote better side effect management, disease symptom management, reducing the chance of E&A admissions, overnight hospital stays. You can improve compliance with treatment regimens, etc. That brings about huge efficiencies and benefits to the health system.” R73
		Health systems need to incentivise healthcare providers to collect data	#141: “That's a technology problem and an incentives problem.” R75
Relative priority The degree to which implementing and delivering the innovation is important compared to other initiatives	Industry	Collecting PROs is deprioritised through most of the drug development process until reimbursement starts to be discussed	#142: “I would shout with my flags: You need to do mixed methods, you got to be qualitative. They would never invest in it. Because they're too busy focusing on the primary and secondary endpoints. PROs come in as exploratory or lower secondaries. They are never powered sufficiently to get the data that you need to say anything of any value anyway.” R35 #143: “You're trying to get it out to the prescribers, to the patients to the markets - so good price, then it's critical we have this data. And then suddenly there is this little gap from marketing authorisation to that. It's like: quick, quick, everybody run around and get this data, because now we need it. We're not going to even get the product over the line if we don't have essential data, especially in Europe.” R35

Incentive systems The degree to which tangible and/or intangible incentives and rewards and/or disincentives and punishments support implementation and delivery of the innovation		Incentives for drug development groups are closely linked with obtaining market authorisation, which is rarely dependent on PROs	#144: “Those groups (…) have got different endpoints they're trying to meet, and they are just trying to get that marketing authorisation.” R35
Mission alignment The degree to which implementing and delivering the innovation is in line with the overarching commitment, purpose, or goals in the Inner Setting		Companies need to see that RWD can help with their business objectives	#145: “I think drug companies need to see success stories. And when they will see drugs being approved, OK now I'm willing to put my toe in the water and take the risk.” R30
Funding The degree to which funding is available to implement and deliver the innovation		Efforts are needed to convince a company to sponsor the study	#146: “It's always a challenge to actually get a real-world study invested in and respected.(…) I'll propose a real world study and people will not understand the value of that.” R35
Patient-centeredness The degree to which there are shared values, beliefs, and norms around caring, supporting, and addressing the needs and welfare of patients	Payer	Payers seek to know more about patient experience	#147: “There's a lot more emphasis now on trying to get a broader sense of patient perspectives and experiences of the condition. So it's not just about that sort of cost per QALY type evidence, but also about patient experience to complement that evidence.” R80
Compatibility The degree to which the innovation fits with workflows, systems, and processes		Standards describing the value of RWE in reimbursement decision-making are needed to fully incorporate their use	#148: “For the use of PROs to kind of supplement (…) evidence, you might want a bit more clarity on exactly how that's going to be incorporated into the decision, what way it is going to be used. To kind of make people more confident that this data when it's collected is actually going to be used to improve care.” R80

Relative priority The degree to which implementing and delivering the innovation is important compared to other initiatives		Mandating PRO data collection as part of managed entry agreements can be the most immediate implementation of PROs	#149: “The area (…) where we are most actively using real-world evidence sort of routinely is in managed access. So that's probably the place to start.” R80
IT infrastructure The degree to which technological systems for tele-communication, electronic documentation, and data storage, management, reporting, and analysis support functional performance of the Inner Setting	Regulator	Regulators need access to RWD databases	#150: “But in the future, we'll probably have something that is more direct, so for DARWIN EU will have direct access to some of these data to the analysis” R26
Work infrastructure The degree to which organization of tasks and responsibilities within and between individuals and teams, and general staffing levels, support functional performance of the Inner Setting		Pre-authorisation RWE applications	#151: “When you have a drug submission in the pre-market area we consider real-world evidence as part of the (submission). It is seldom the pivotal piece of evidence, but it can be very complimentary to, for example, a clinical trial. (…) So, that's where it can help to inform that, but again the real-world evidence is just a piece of the puzzle.” R83
		Post-authorisation RWE applications	#152: “In the post-market environment, (…) if we're looking at information that we got through the vigilance database, we may supplement that also by looking through the literature or by initiating a drug safety and effectiveness network study with research teams, where we can collect that information. It provides that additional information so that we do get the patient perspective of their experience to take that into consideration in our decision making.” R83
Patient-centeredness The degree to which there are shared values, beliefs, and norms around caring, supporting, and addressing the needs and welfare of patients		Regulators seek to know more about patient experience	#153: “Regulators want to know what the patients really think and feel about a particular health condition. So, they're very important, in that way.” R100

Learning-centeredness The degree to which there are shared values, beliefs, and norms around psychological safety, continual improvement, and using data to inform practice		Regulatory bodies need to keep up with evolving field	#154: “There wasn't all that much new stuff (…)happening, but in the last 20 years it's been a lot of new developments. Things being borrowed from other fields: education, psychology etc.” R100
Compatibility The degree to which the innovation fits with workflows, systems, and processes		Extremally rare use of PROs for regulatory decisions	#155: “I think the main issue is just the lack of experience of using that data. It's something that we very, very rarely do. I mean, extremely rarely do. Even in clinical trials, often patient-reported outcomes are exploratory endpoints. And exploratory endpoints in most cases are not going to influence a regulatory decision.” R85
		Standards describing the value of RWE in regulatory decision-making are needed to incorporate their use fully	#156: “From a regulatory perspective, it's quite hard to know how to use that data or make recommendations how to use that data” R85
Relative priority The degree to which implementing and delivering the innovation is important compared to other initiatives		PROs collected in real-world can be used in the first instance for tolerability and safety monitoring	#157: “Now, in post-authorisation (set-up) we do have to rely on RWD, because the study is done, finite, it's close. So we need to see what's happening outside that clinical design environment and that's where RWD has a little bit better foot on the ground.” R26
		PROs collected in the real world can contribute to label expansion decisions	#158: “So I think about patient focus drug development and label expansion. I think we should be thinking about including more patient experience data that are generated from the real world.” R75
Mission alignment The degree to which implementing and delivering the innovation is in line with the overarching commitment, purpose, or goals in the Inner Setting		PROs can help to systematically answer regulatory questions	#159: “We couldn't support systematically our Committee in the decision-making, if we had no access to PROs. We could do it if we have access to primary care, secondary care (data), etc., and we can improve that answer through PROs. It wouldn't be the main source (though) for a systematic answer.” R36

IV. Individuals domain			
Motivation The degree to which the individual(s) is committed to fulfilling Role	Hospital managers	Hesitation to invest in PRO data collection at the hospital level, especially when future savings are uncertain	#160: “Business managers are not keen to pay, even we're talking about 20-30,000 GBP which, for a bit cancer hospital, isn't a lot actually. But they're not willing to do that. So, I think this is a barrier.” R2
Capability The degree to which the individual(s) has interpersonal competence, knowledge, and skills to fulfil Role	Industry employees	Lack of knowledge about the value of PROs	#161: “I had to educate every time I was in a new team. I had to educate people about the value of PROs. I think it's sort of a unique field that sort of more comes out of psychology or some other sort of ancillary field to medicine.” R100
Motivation The degree to which the individual(s) is committed to fulfilling Role		Involve PRO champions in drug development teams	#162: “You can put your PRO specialist into the trial development and they'll keep banging on the door to get this done. Because it's important for their objectives. They probably won't get a label claim, which will be probably how they will be judged, because that's always ends up being too far down on the list of clinical trial endpoints. But the rest of the team might not be at all focused (on it), they will be more core scientists who are looking at like safety endpoints and biometric stuff they really need to show it is efficacious.” R35
Capability The degree to which the individual(s) has interpersonal competence, knowledge, and skills to fulfill Role	Statisticians	Statistician involvement less present in the real-world setting	#163: “The clinical trial by default comes with statisticians. Statisticians that have knowledge how to impute data. How to improve the quality of data, how to account for potential biases or limitations of the data sets, how to set up the sample size so your findings are reliable.” R26

Opportunity The degree to which the individual(s) has availability, scope, and power to fulfill Role		Statisticians are often focused on other types of outcomes	#164: “Often, especially if the drug doesn't succeed or on the other hand, if it is succeeding and there's a rush towards launch, there aren't the resources to analyse the PRO data. I think that's probably changed since I left the industry, but it's may still be there.” R100
Opportunity The degree to which the individual(s) has availability, scope, and power to fulfill Role	PRO researchers	Not enough PRO experts	#165: “I definitely don't think we have enough people. I feel that our PRO world is very niche. There's only a small group of us.” R8
Capability The degree to which the individual(s) has interpersonal competence, knowledge, and skills to fulfill Role		Lack of epidemiological knowledge, which is essential to interpret real-world studies correctly	#166: “Not all PRO researchers have a background in epidemiology. That's needed to understand bias and all these things. I mean, epidemiology is really all about real-world studies.” R100
Opportunity The degree to which the individual(s) has availability, scope, and power to fulfill Role	IT specialists	IT specialists too busy with other projects, so challenging to get their attention on the PROs collection	#167: “They're just overwhelmed. I could offer them $50,000 but it wouldn't get me very much and it's not going to pay for long-term solutions.” R12
Need The degree to which the individual(s) is committed to fulfilling Role	Administrative staff	The needs of admin staff to help with better questionnaire administration should be identified	#168: “But no one ever really bothered to check with the front desk people about what would be helpful to them.” R91

Capability The degree to which the individual(s) has interpersonal competence, knowledge, and skills to fulfill Role		The quality of collected data depends on them	#169: “It entirely depends on the staff at the site completing the data of patients actually doing PROs.” R35
Opportunity The degree to which the individual(s) has availability, scope, and power to fulfill Role	Nurses	They can play an important role in data collection, but training needs to be offered	#170: “I think nurse practitioners are probably going to allies. (…) Because they're just have a higher touch rate with patients than the physicians and probably way you can get some culture change. But yeah, I do think you do need to have education…” R30
		Some resistance can be seen to the extra work associated with data collection	#171: “Patients were happy to fill it out. It was just that the nurses were the one that were objecting to it – it takes too much time, patients are so burdened. That's not true, patients actually didn't have a problem with it. It was them who had the problem.” R100
Capability The degree to which the individual(s) has interpersonal competence, knowledge, and skills to fulfill Role	Physicians	Variable level of PRO knowledge between different areas of medicine	#172: “I don't know that physicians are trained in use of PROs now. I will also say that I've worked in some areas, for example, urology, where PROs are really the primary endpoint, right? So, they really understand PROs.” R100
		Most physicians have problems with the interpretation of complex PRO concepts	#173: “And what do these scales and scores really mean? And can you generalise them? There's a very nuanced background that you need.” R74
		IT tools can flag to physicians reports, which need their attention	#174: “The massive benefit of ePROs is (…, that) we can use technology to say: OK, (…) which of the responses have changed and let's flag that one, which of the responses is significantly worse - let's flag the one as well.” R41
		Should be offered training on data collection	#175: “I think they might need some training as well, right? In terms of how to record, make sure that they are collecting these outcomes in an appropriate manner.” R83
Opportunity The degree to which the individual(s) has availability, scope, and power to fulfill Role		Lack of physician buy-in impacts the completeness of data	#176: “That's just a mindset of some clinicians that PROs don't add value to their practice. (…) So that increases the missing data, because, eventually, their patients stop filling them in, because they realise that the clinician isn't interested in looking at them. So they stopped filling them in. This is well described phenomenon. That's a problem. So, the clinician’s willingness to collect data in practice gets in the way of using those data in real world evidence…” R12

		Too many PRO alerts put-off clinicians from using it. Smarter algorithms are needed	#177: “I also think we need to get much smarter about alerts in electronic health record systems. So, i'm working with a new clinic (…) they're pushing back, because they don't like how many alerts they get. So, they get alerts for fatigue, which is not helpful.” R91
Motivation The degree to which the individual(s) is committed to fulfilling Role		Co-designing the study increase motivation	#178: “Inviting them to be co-developers could help from the beginning. If it's a top-down kind of thing, I think they're going to be more resistant.” R91
		Concerns about prolonging consultation	#179: “And then minimal involvement, I think, for clinicians is key. At least for oncologist. They will appreciate it, when they have access to the data. But that's probably not their highest priority, whether it prolongs the consultations and although I have data showing these things don't prolong consultations, that's still the highest concern about it.” R2
		Perception of PRO value determines willingness to collect PROs	#180: “For the healthcare professionals, it depends on what they see as the value of collecting that data and if it's for subsequent use by someone like NICE in order to make decisions, it might seem to have slightly less relevant than using it for direct sort of clinical care, but obviously keeping them informed and getting buy-in about the purposes of this collection and why it's important (is key).” R80
		To improve care at the individual level	#181: “They're collecting it as part of clinical practice, so they're trying to derive benefits in their practice, either on the day of the encounter or monitoring people between visits. But their mindset is, how can I improve the care of this patient, not how can I do a research project.” R12
		To identify patients who need help	#182: “Many of them think it will help reduce patients coming to hospitals, long waiting lists, etc. While still help identify patients who need help and others that can self-manage.” R2
		To find out how treatment affects patients	#183: “I think they would want to, because I think, they know it would help them know how their patients are doing.” R8
		Champions help to convince other HCPs about PROs’ value	#184: “You need somebody in the clinic who believes in this, like a leader who believes in this. (…) You need somebody in there, showing that this has value for something (…) and then, others will come along. (…) You really have to be (…) passionate about it.” R30
Need	Patients	PROs help to inform about individual’s needs in broader perspective	#185: “We need to think about different ways of measuring some of those things to include with PROs, so things like climate change that affects her health, environment, the psychosocial stuff that affects us on a day-to-day basis.” R21

The degree to which The individual(s) is committed to fulfilling Role		PROs put patients at the center	#186: “Well, if we're putting patients at the center, we need to understand and learn about the patient and what their needs are.” R21
		PROs inform about the subjective impact of the disease on the patient	#187: “Somebody feels more or less pain, everyone's perception of things is different, and that's OK as well. But (…) maybe others could manage in that situation. But that person can't. (…) That just justifies that they need a bit of extra help or whatever, and that's the whole point of patient report rather that the ticking boxes.” R16
Capability The degree to which the individual(s) has interpersonal competence, knowledge, and skills to fulfill role		Need to find a balance between burden to the patient and collecting information of interest	#188: “Again, my concern all the time is to try and minimise the amount of time patients have to commit to complete questionnaires while still getting the data you need. And I think that's forever a challenge.” R40
		Irrelevant questions asked repeatedly pose an enormous burden to patients	#189: “Our experience is that the number of questionnaires is not actually normally a burden, burden is irrelevance of questions when they don't fit the circumstances in which they're being used. Often, they're too generic and therefore patients are being asked questions that just don't fit their situation.” R41 #190: “One of the biggest things we hear from the burden perspective are people filling in the same questions where they're irrelevant, and when nothing has changed.”R41
		Computer adaptive testing (CAT) can reduce patient burden by asking more relevant questions	#191: “One of the things I'd like to see adopted more is a computerised adaptive testing.” R100
		Using PROs for some people can be easier than talking about their health	#192: “Sometimes people will prefer to write it down rather than speak about it, because some people find it difficult to speak about their illnesses.” R3
		The level of IT literacy needs to be considered when planning electronic data capture, but most of the responders should be able to use technology	#193: “Over recent years, the percentage who would not use technology at all has significantly decreased, and that's across all age groups. And obviously, that's cultural and country-dependent. So, I think the first point to say is not to overestimate the group that you assume would ask for a hard copy. Often, it's actually not the case. And even in the oldest age groups.” R41

Opportunity The degree to which the individual(s) has availability, scope, and power to fulfil role		People should be given an appropriate amount of time to respond. Remote data collection help with that.	#194: “There is more flexibility with (electronic data capture).” R16 #195: “Once you've got your own time to read it and think about it, and do it, rather than (…) trying to do at the doctors so they're waiting for you to do it. And I know, sometimes the first answer - quick ticks are best, but sometimes you think: Well, hang on a minute! What? How does that affect me? And if there's more thinking, that needs to go to it... So, I think (…) if you've got that on an app that you can do it at home (it helps).” R16
		HCP buy-in impacts patient’s commitment to data provision	#196: “I think doctors can do a lot of encouraging and unconscious discouraging at times, so what you want is, you want the clinicians who are going to be giving the questionnaires to be very committed to the idea that they're gathering valuable data.” R40
Motivation The degree to which the individual(s) is committed to fulfilling role		Patients are generally happy to complete PROs	#197: “Patients are very keen to be listened to if they have something like I am diagnosed with something, even a little thing or I have a fever or something. ”R26 #198: “The cancer patients are generally willing to contribute and participate. They're grateful that we look after them.” R2 #199: “They want someone to hear their experience.” R8
		Altruistic motivation to help with research and improve the care of others	#200: “But to me and for many sharing data if it helps somebody, or if it helps, enables research, they would do it.” R3
		Being informed about the purpose of data collection and study progress increases willingness to participate	#201: “If they got a proper understanding of why the information is being collected and how it could possibly help them going forward as part of their treatment.” R18
		Patients need to be reassured that their data are safe	#202: “There’s like the privacy question: where's my data going and all that sort of things.” R16
		Lack of trust, especially among underserved populations	#203: “In the US there are groups of folks that have trust issues with healthcare, so they will be more hesitant and we know that, we are very much aware of that and we try to work with that.” R8

		Co-designing the study increases willingness to participate	#204: “We try to design studies that are really patient relevant and meaningful by using patients in our design phases. And so, we've changed the modality in which we collect that data also to make sure that it is fit for purpose and relevant to the groups. So, I think it's designed in that way you're reducing your challenges in that domain.” R35
		Results should be fed back to the patients	#205: “And I think what I really want to see more of, is being involved from the beginning to see it through right until the end and get the results. Often that doesn't happen. You fill something out. That's it. No feedback…” R3
		The fact that PRO will be used to inform their care is increasing motivation to participate	#206: “I am interested in providing this personal information because I understand that my care is going to be better and my health probably will improve or my survival would be lengthened.” R99
V.	Implementation process domain (The activities and strategies used to implement the innovation. Distinguish the implementation process used to implement the innovation (activities that end after implementation is complete) from the innovation (the “thing” that continues when implementation is complete)		
	Implementation priority setting	HCPs should point out populations and settings where PRO data collection can bring the most significant benefits.	#207: “We think it's the best (if it comes) from the clinician that, they see a place where it is good to use PRO. It's better than when it comes from top to bottom,” R25
	Pilot studies	Conduct pilot studies to identify the most important barriers	#208: “I think there are groups who are doing these sort of pilot studies to try and show, and even if you can't get a fully useful thing (…) you can sort of show where the pain points are.” R30
	Sustaining benefits in the long-run	Create a sustainability plan to retain the long-term effects of PRO implementation	#209: “Present a project as an initiative that is there to stay with a clear sustainability plan (…) Almost like a plan, these are the inputs, this is what I'm going to do. I need this type of support from you, the cost of that support, so if it can have an estimate right. And then, these will be the outcomes and then the most proximal outcomes will be X. And then long-term outcomes.” R99
	Setting up standards for PRO data collection	Data collection in routine care needs to be carefully planned and agreed upon	#210: “It starts with a vision and a program and then, you can ask: do we have the right IT to support this program? Right now there's no vision, there's no program. There's just a desire to collect PROs in clinic and then maybe use them in the real world, but that's too soften and mushy. You don't get quality data with an opportunistic approach.” R12
	Instrument design	Platforms for ePRO data collection need to be user-friendly and work across different types of devices and operating systems	#211: “Make sure whatever software we use, it works across different kinds of devices” R41 #212: “So they need to be simple, precise, really.” R21

		PRO questionnaires usability should account for different disabilities patients might have	#213: “Yellow and green highlight is very good for visually impaired people.” R3 #214: “And link to an audio that can speak it over like: “Question one”, and you can hear somebody literally hear what question one is.” R3
		Automatic reminders should be used to increase completion rates	#215: “And one important thing to make it easier - send reminders. Otherwise, people forget. So, if you want that data regularly, you have to remind them.” R2
	Instrument selection	Validated PRO instruments should be used if exists. If not, additional work needs to be done to check their measurement properties	#216: “Whether it's even valid in the population, you're always going to have that. You might have done some legacy work, like we've done work to show that, even though our PROs are not disease specific, we've done quite a lot of work on the psychometrics to show that they are actually robust and reliable and valid within our population.” R35
		PRO instruments need to be able to address the research question	#217: “I think it very much depends on the research question. Always your research question should address what problem or what questions you want to answer and then you would map you methodology and your endpoints and instruments to that research questions.” R85
		PRO instruments need to ask questions which are relevant to the patients	#218: “Questionnaires need to be brief. (…) You don't want to go: not applicable, not applicable, not applicable, not applicable, through a whole stream of questions. That 's discouraging.” R40
	Engaging	Engage stakeholders across the board Consider their involvement in the co-design of the study and target them with various educational endeavours	#219: “I think it's going to take educating, and I say this because we were confronted with this right now ourselves. It is educating about what is your purpose, how do you make a thoughtful approach.” R8
		Buy-in from health institutions is key for successful implementation	#220: “The main barriers are, we know, the institutions - the health institutions that are quite rigid and the time. So, because the institutions are very rigid it takes time to break that, you know, to soften up the rigidity and allow for these things to be integrated” R99

	Type of RWE studies with highest potential to use PRO data successfully	Start with prospective data collection and focused research question	#221: “I think, the secondary uses is harder, maybe just have too much noise, too many unknowns.” R30 #222: “Well, you don't just go out and gather vast quantities of data for the sake of it. You know that's a pointless exercise. You achieve very little. When (…) you prospectively gathering data, you know the purpose you are aiming to put that data. So, you don't want big, loose general questionnaires. You want focused questionnaires.” R40
		Start with secondary use of data collected in routine care	#223: “I just think that to me the implementation and the integration of patient reported outcomes and patient reported experience outcomes into the healthcare systems to inform quality improvement, research, management is a given and it's happening. And then the use of this information, once you have it, through the health care system why the pharma companies need to go back and collect it?” R99
		Start with post-authorisation safety monitoring	#224: “I think it's important to say that the setting of where RWE can have an impact, currently is mostly in the post-authorisation setting where drug has already got a marketing authorization.” R85
	Setting up standards for the use of RWE	Decision-makers need to show that RWD are used and expected	#225: “I think it's like a concerted effort by decision makers, by FDA, by an HTA, by payers to say: we are using this information and we actually expect it.” R75
		The value of RWD need to be demonstrated by practice-changing studies	#226: “I think people need to see the added value of it. And it's not been shown yet. So, any of those things that can all be done at the same time. Consensus - right to standards and then you know practice changing studies that can be shown to everybody.” R74
		Decision-makers need to know how RWE can influence their decisions. Case studies would be helpful	#227: “Then it seems a bit we have it funny for us to encourage data collection, that we didn't understand how it might influence our decision making, so that'd be a reluctance from industry to spend the money. I think it's a bit chicken and egg and I think it comes back down to, you know, which I keep going on about i'm afraid, but it is about having some good examples about where the collection of PRO in real world evidence has made a difference. Because until you can demonstrate that it's added value or it actually has a use, then I don't think the field is going to move on, because there's no incentive or motivation for it to move on.” R85