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How to Collect PROs in RW Studies and Leverage Them for Robust Evidence Generation?

ISPOR Good Practices Task Force on Patient-Reported Outcomes (PROs) in Prospective Real-World Studies: Emerging Recommendations & Next Steps

ISPOR RWE SUMMIT 2025 – Tokyo, Japan
Workshop
September 29, 2025

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SECTION

1

Welcome and Introductions

Moderator & Speakers

Konrad Maruszczyk (Moderator)
Research Fellow, Centre for Patient Reported Outcome Research, University of Birmingham, Birmingham, UK

Jessica Roydhouse (Speaker)
Senior Research Fellow, Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia

Kirsten Howard (Speaker)
Professor of Health Economics, Leeder Centre for Health Policy, Economics and Data, University of Sydney; Chair of Economic SubCommittee of PBAC, Australia

Antony Martin (Speaker)
Sr Research Scientist, CEVR, Tufts Medical Center; Director, QC Medica LLP; Honorary Research Fellow, University of Liverpool

Agenda

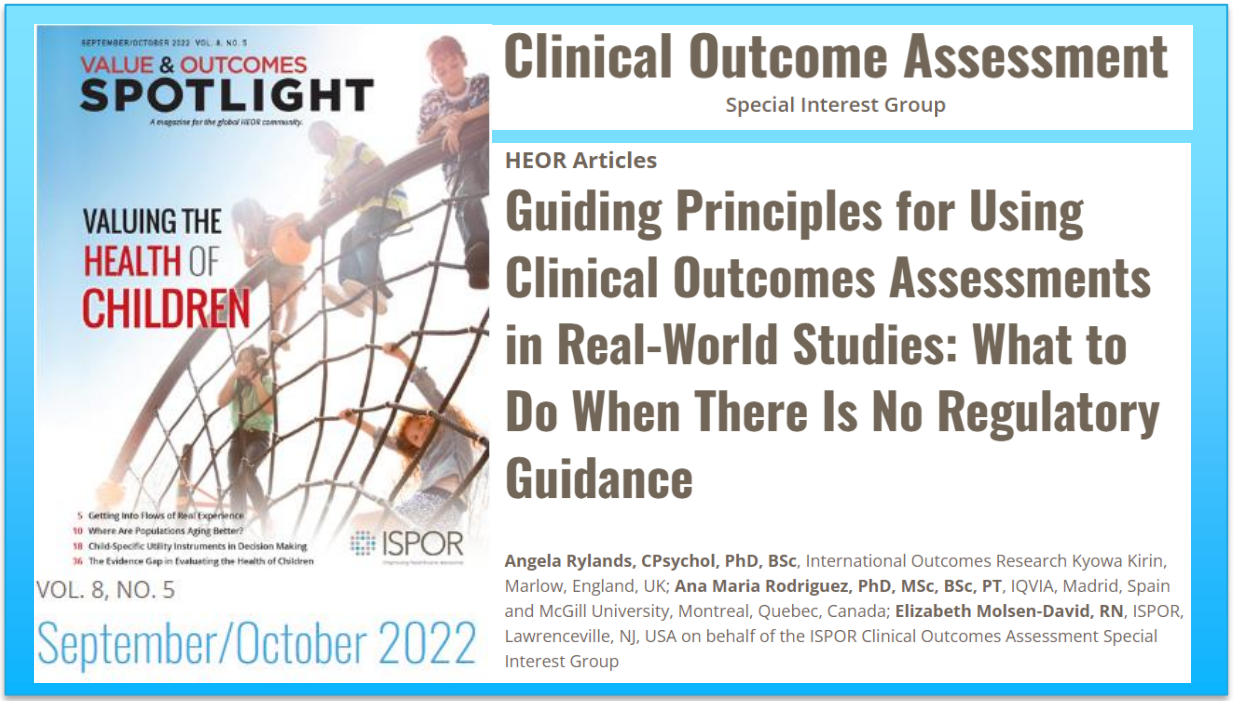
1. Welcome & Introductions
2. Background to this Task Force
3. Task Force Emerging Recommendations
4. The role and value of RW-PRO - Decision Maker Perspective
5. Prospective RW-PRO studies and HTA - Industry Perspective
6. Audience participation

SECTION

2

Background to Task Force

COA SIG: Need for RW-PRO Guidance



- ISPOR's COA SIG conducted a piece of work to address this through a membership engagement project that included:
- ISPOR member survey
- Expert round table presentation

Publications Calling Out the Need for Guidance


Maruszczyk et al.
Journal of Patient-Reported Outcomes (2022) 6:57
https://doi.org/10.1186/s41687-022-00466-7

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 Aiy
Thomas Keeley[1,6] and Melanie J. Calvert[1]


nature reviews drug disc

COMMENT

Harnessing the patient voice in real-world evidence: the essential role of patient-reported outcomes

Melanie J. Calvert[1]*, Daniel J. O'Connor[2] and Ethan M. Basch[3]


Heliyon 9 (2023) e20157

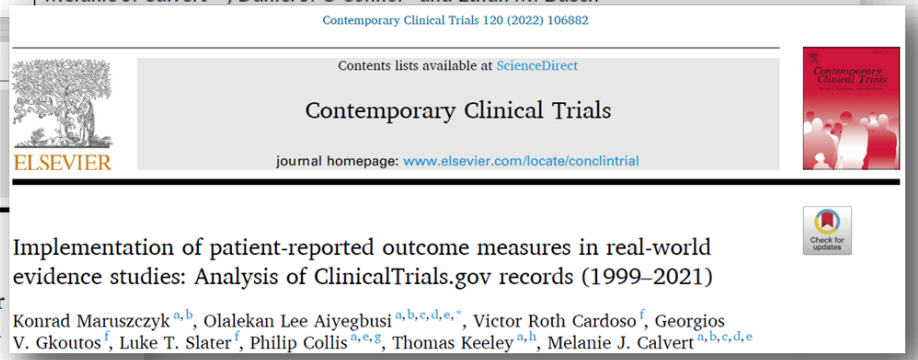
Contents lists available at ScienceDirect

Heliyon

journal homepage: www.cell.com/heliyon

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]


Contemporary Clinical Trials 120 (2022) 106882

Contents lists available at ScienceDirect

Contemporary Clinical Trials

journal homepage: www.elsevier.com/locate/conclintrial

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]

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Task Force Membership

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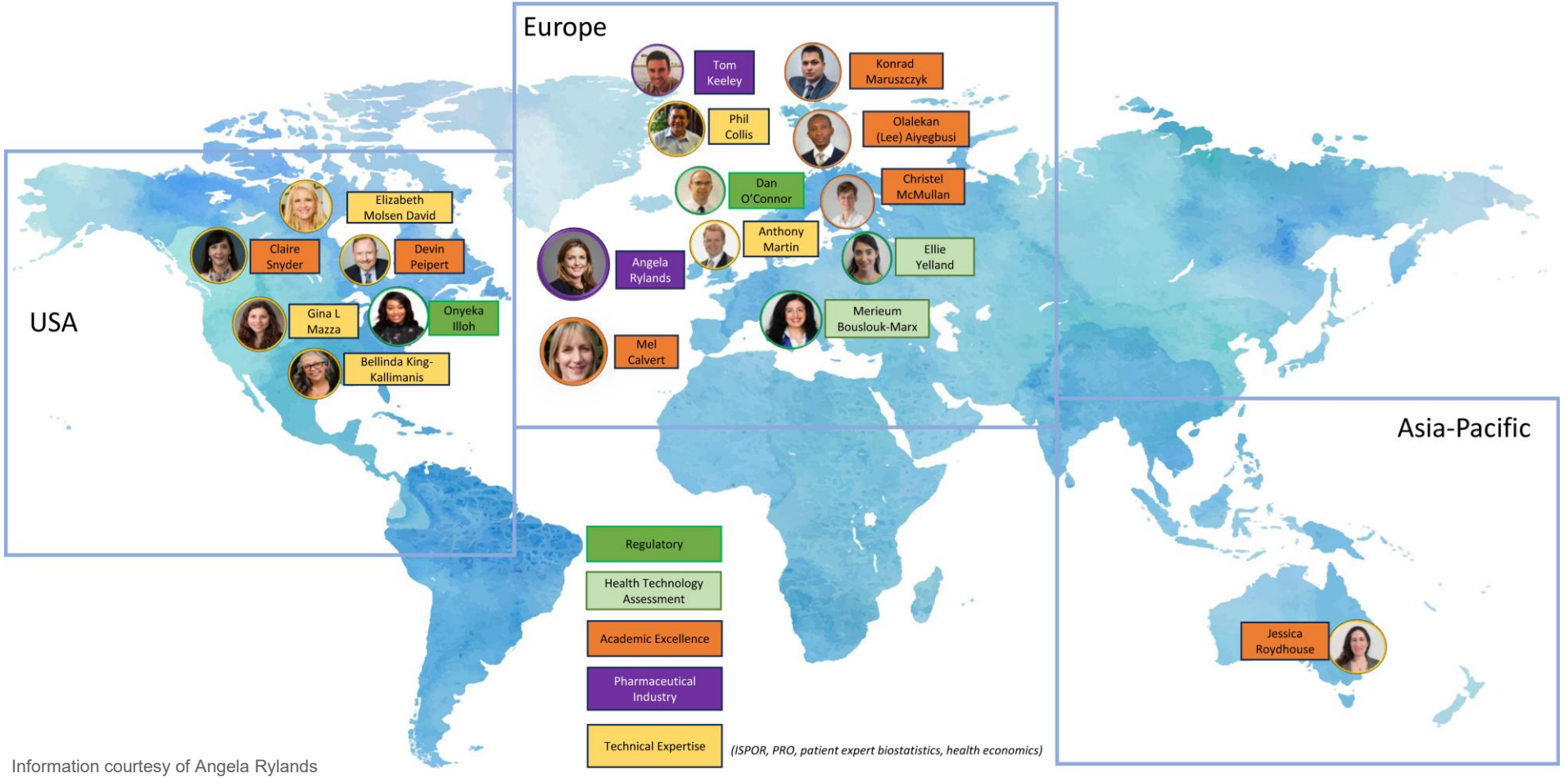


Information courtesy of Angela Rylands

Available RWE & PRO Guidance

www.ispor.org

RWE Guidance (examples)

FDA U.S. FOOD & DRUG ADMINISTRATION
FRAMEWORK FOR FDA'S REAL-WORLD EVIDENCE PROGRAM 2018

Real-World Data: Assessing Electronic Health Records and Medical Claims Data To Support Regulatory Decision-Making for Drug and Biological Products
Guidance for Industry
DRAFT GUIDANCE
2021

Real-World Data: Assessing Registries to Support Regulatory Decision-Making for Drug and Biological Products
Guidance for Industry
2021

Data Standards for Drug and Biological Product Submissions Containing Real-World Data
Guidance for Industry
2021

Considerations for the Use of Real-World Data and Real-World Evidence to Support Regulatory Decision-Making for Drug and Biological Products
Guidance for Industry
2021

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH
Real-World Evidence in EU Medicines Regulation: Enabling Use and Establishing Value
2022

2022

DARWIN EU
2023

cadth acmts
Canada's Drug and Health Technology Agency
L'Agence des médicaments et des technologies de la santé au Canada
Guidance for Reporting Real-World Evidence
2023

ISPOR
Wang et al. 2023
HARmonized Protocol Template to Enhance Reproducibility of hypothesis evaluating real-world evidence studies on treatment effects: A good practices report of a joint ISPE/ISPOR task force

PRO / COA Guidance (examples)

FDA U.S. FOOD & DRUG ADMINISTRATION
Guidance for Industry
Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims
U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
December 2009
Clinical/Medical
2009

FDA U.S. FOOD & DRUG ADMINISTRATION

2017

ISPOR Task Force Publications in COA

(1) Wild et al. 2005
Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: Report of the ISPOR Task Force for Translation and Cultural Adaptation

(2) Wild et al. 2009
Multinational Trials—Recommendations on the Translations Required, Approaches to Using the Same Language in Different Countries, and the Approaches to Support Pooling the Data: The ISPOR Patient-Reported Outcomes Translation and Linguistic Validation Good Research Practices Task Force Report

(3) Coons et al. 2009
Recommendations on Evidence Needed to Support Measurement Equivalence between Electronic and Paper-Based Patient-Reported Outcome (PRO) Measures: ISPOR ePRO Good Research Practices Task Force Report

(4) Rothman et al. 2009
Use of Existing Patient-Reported Outcome (PRO) Instruments and Their Modification: The ISPOR Good Research Practices for Evaluating and Documenting Content Validity for the Use of Existing Instruments and Their Modification PRO Task Force Report

(5) Patrick et al. 2011
Content Validity—Establishing and Reporting the Evidence in Newly Developed Patient-Reported Outcomes (PRO) Instruments for Medical Product Evaluation: ISPOR PRO Good Research Practices Task Force Report: Part 1—Eliciting Concepts for a New PRO Instrument

(6) Zbrozek et al. 2013
Validation of Electronic Systems to Collect Patient-Reported Outcome (PRO) Data—Recommendations for Clinical Trial Teams: Report of the ISPOR ePRO Systems Validation Good Research Practices Task Force

(7) Matza et al. 2013
Pediatric Patient-Reported Outcome Instruments for Research to Support Medical Product Labeling: Report of the ISPOR PRO Good Research Practices for the Assessment of Children and Adolescents Task Force

(8) Eremenco et al. 2014
PRO Data Collection in Clinical Trials Using Mixed Modes: Report of the ISPOR PRO Mixed Modes Good Research Practices Task Force

(9) Walton et al. 2015
Clinical Outcome Assessments: Conceptual Foundation—Report of the ISPOR Clinical Outcomes Assessment – Emerging Good Practices for Outcomes Research Task Force

(10) Powers et al. 2017
Clinician-Reported Outcome Assessments of Treatment Benefit: Report of the ISPOR Clinical Outcome Assessment Emerging Good Practices Task Force

(11) Benjamin et al. 2017
Patient-Reported Outcome and Observer-Reported Outcome Assessment in Rare Disease Clinical Trials: An ISPOR COA Emerging Good Practices Task Force Report

(12) O'Donohoe et al. 2023
Updated Recommendations on Evidence Needed to Support Measurement Comparability Among Modes of Data Collection for Patient-Reported Outcome Measures: A Good Practices Report of an ISPOR Task Force

(13) Edgar et al. 2023
Recommendations on the Selection, Development, and Modification of Performance Outcome Assessments: A Good Practices Report of an ISPOR Task Force

Information courtesy of Angela Rylands

Defining RW-PRO....

- Patient reported outcome (PRO) data generated for RWE is often collected in post-authorization studies conducted to support labelling claims, reimbursement and health policy, but in certain instances, pre-approval.
- The terminology around RW-PRO is not yet defined nor is it uniformly described.
- ***We would like to define RW-PRO studies***, their purpose, and to consider these to include:
  - Pragmatic studies (e.g. assessing effectiveness of treatment [phase 3b and phase 4)
  - Registries
  - Retrospective data analyses
  - Observetional studies
  - Surveys

Purpose of the Task Force

Patient Reported Outcomes (PROs) in Prospective Real World Study Design

Objective: To enhance the robustness and transparency of RW-PRO research

Scope:

- To describe the value of RW-PRO research, identify and summarize existing guidance
- To highlight emerging good practices, identified through TF member discussion
- The emerging good practice recommendations will concentrate on prospective RW studies aimed at generating patient-level data

SECTION

3

Task Force Emerging Recommendations

Jessica Roydhouse, PhD
Senior Research Fellow
Menzies Institute for Medical Research,
University of Tasmania

RW-PRO Focus Areas

- Study objective
- Patients as partners
- Study population
- Data quality
- Implementation
- Analysis
- RW-PRO
- Technology
- Regulatory and HTA Engagement

Develop a clear and feasible study objective(s)

- Important for any study
- Feasibility: consider RW context

Working with Patients as Partners

- Important for any study
- Engage early
- What to address
  - Research questions: relevance, importance
  - PRO measure selection
  - PRO collection schedule
  - Communicating study value
  - Inclusive data collection

Working with Patients as Partners: What is Needed

- Clear understanding of study purpose
- What is the partner's role, how does it fit within the study

Working with Patients as Partners

- Input and preferences about proposed design
- Consider work to validate selection of PRO items or support concepts of interest
- Develop strategy to work with patients as partners

Study Population

- How might the RW environment affect sample size and sampling methods?
- Who can provide data?

Study Population

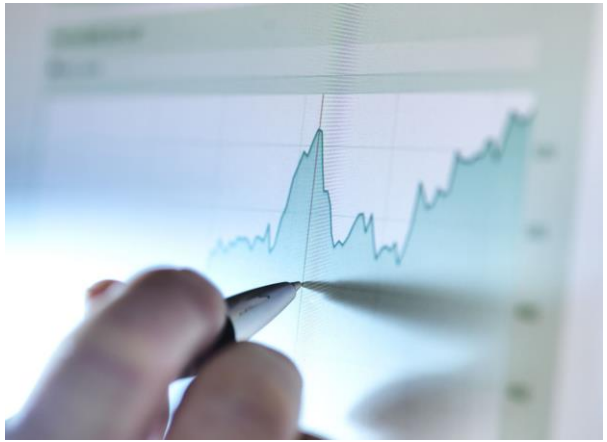
- Define target population
- Define disease or condition
- Define participation criteria
- Consider aspects related to therapeutic area
- Determine sample size, sampling methods
- Participant willingness and ability to participate

RW-PRO

- Psychometrics
- Modification
- Appropriateness
- Feasibility

Data Quality

- Develop long-term monitoring procedures
- Develop a plan for quality control and monitoring
- Implement ongoing data audit: multiple levels
  - Individual questionnaire
  - Individual patient
  - Healthcare provider
  - Entire study
- Minimise respondent and clinical staff burden



Implementation

- Identify optimal context
- **Mode of instrument: further investigation required?**
- Develop strategy to maintain participant willingness to participate
- Partner with clinical staff to incorporate data collection into workflow
- ISPOR Updated Recommendations – Mode of PRO Data Collection

https://www.ispor.org/heor-resources/good-practices/article/updated-recommendations-on-evidence-needed-to-support-measurement-comparability-among-modes-of-data-collection-for-patient-reported-outcome-measures

Analysis

- Timing of assessments
- Confounding
- Loss to follow up
- Missing data
- Context
- Interpretation

Technology

- Existing workflow
- Data integration
- Equity
- **Modes**
- Electronic data capture
- Support

Regulatory & HTA Engagement

- Engage early!

SECTION

4

The role and value of RW-PRO Decision maker perspectives

Kirsten Howard, PhD
Professor of Health Economics,
Leeder Centre for Health Policy, Economics and Data
University of Sydney

Chair, Economic Sub Committee of PBAC and Member PBAC

Outline

1. The value of consumer input to PBAC
2. What type of consumer input is most useful to help PBAC decision making
3. Potential value of RW-PRO to PBAC
4. Comment on Recommendations

VALUE OF CONSUMER INPUT TO PBAC

- Consumer input is important because it helps PBAC better understand people's experience with the health condition and treatments

  - how a health condition affects people's lives (and that of carers and family)
  - how current treatments affect people's lives (and that of carers and family)
  - how the proposed medicine might affect the lives of people with the health condition, their carers, and families.

WHAT IS MOST USEFUL TO HELP PBAC IN DECISION MAKING

1. Lived experience of the health condition and how it affects your life, and the life of family and carers
2. Lived experience of current treatments – positive and negatives, impacts on daily life, e.g., side effects, access issues, etc.
3. Any experiences of the new medicine under consideration
   - How has it impacted on your condition, your daily life, your quality of life?
   - What adverse effects did you experience?
   - Are there differences in access to this medicine compared to other treatments?

     E.g., is it easier to take because it is oral, compared to other IV treatments? Is it given less often and how has this impacted your life?
4. What are your perceived benefits and disadvantages of this new medicine compared to current treatments (if no personal experience)?

POTENTIAL VALUE OF RW-PRO IN HTA

- Patient experience/PRO of the health condition; also carer/family
- Patient experience/PRO of current treatments – as HTA is comparative – e.g. PBAC has a legislative requirement to consider comparative efficacy, safety and cost – need to understand PRO for current treatments
- Any patient RW experience of the medicine being considered
- Relationships between PRO and clinical outcomes
  - Modelling/economic analysis/utilities
- Understanding RW impacts on patient outcomes – PRO and clinical, post-market after reimbursement
  - Also, potentially useful in the context of managed entry/coverage with evidence development reimbursements

TASKFORCE RECOMMENDATIONS

1. **Develop Clear and Feasible Study Objective(s)**: Ensure that the study objective(s) for collecting PRO are clearly defined, feasible and add value.
2. **Working with Patients as Partners**: Engage patients as active partners throughout the research process to enhance relevance, acceptability, and adherence.
3. **Study Population**: Carefully define and select the study population to ensure relevance and representativeness.
4. **Fit-For-Purpose PRO Instruments in RW Settings**: Assess the appropriateness and feasibility of the selected PRO instruments within RW settings.
5. **Data Quality**: Prioritise robust data collection methods and processes to maintain high data quality and integrity.
6. **Implementation of PROs**: Develop clear strategies for incorporating PROs into the study, considering patient pathways, participants' and clinical staff burden.
7. **Analysis of PRO Data**: Design a comprehensive plan for analysing PRO data, ensuring that it aligns with the study's objectives and accounts for potential challenges presented by the RW setting.
8. **Using Technology**: Leverage technology to streamline data collection, improve accessibility, and enhance patient engagement.
9. **Regulatory and HTA engagement:** Engage early with regulators and HTA bodies, to ensure RW-PRO data will meet evidentiary requirements.

DECISION MAKER PERSPECTIVES

- **Working with Patients as Partners**: Engage patients as active partners throughout the research process to enhance relevance, acceptability, and adherence.
- **Fit-For-Purpose PRO Instruments in RW Settings**: Assess the appropriateness and feasibility of the selected PRO instruments within RW settings.
- **Regulatory and HTA engagement:** Engage early with regulators and HTA bodies, to ensure RW-PRO data will meet evidentiary requirements.

- These 3 recommendations are very interlinked for HTA – it is vital that patients and caregivers are engaged to ensure RWE collected is relevant and fit-for-purpose for HTA; not only measures used are fit-for-purpose for HTA, but they collect aspects of RW treatment that are relevant and important to patients and caregivers – What matters to consumers about their treatment and does the PRO capture this? If not, how could other aspects be captured in RWE collection?

- Regulatory and HTA engagement – needs to be unpacked a bit – purpose/usefulness of PROs for regulatory and HTA bodies might be quite different; similarly, the purpose of engagement early might be quite different for regulators and HTA bodies – HTA bodies often need PRO information on new technology and current practice; regulators may just want information on how PRO change with new technology (not comparative); is early engagement to support sponsor submissions?; is it to involve stakeholders in where a therapy will be placed for reimbursement?

- HTA post-market data collection – coverage with evidence development; managed access (payment) arrangements; pay for performance arrangements - may be relevant for choice of PRO

SECTION

5

Prospective RW-PRO studies and HTA

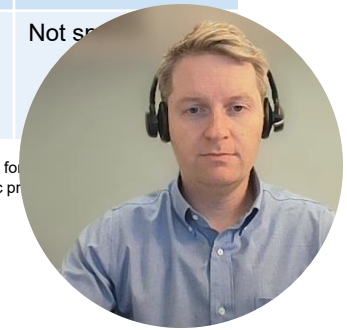
Antony P. Martin PhD MSc
Sr Research Scientist, CEVR, Tufts Medical Center
Director, QC Medica LLP
Honorary Research Fellow, University of Liverpool

HTA Reference Case for Measurement and Valuation of Health Effects

Measurement and valuation of health effects	NICE[1]	CADTH[2] (CDA)	ICER[3]	IQWiG[4]	HAS[5]	PBAC
Instruments with which change in HRQoL should be measured (adult patients)	EQ-5D-3L or EQ-5D-5L*	GPBM	GPBM	Morbidity and HRQoL patient-relevant endpoints	EQ-5D-5L	GPBM
Population in which change in HRQoL should be measured	Patients	Patients	Patients	Patients	Patients	Patients
Preferences (tariffs) with which health states should be valued	UK societal preferences	Canadian (or similar) societal preferences	US societal preferences (and evLYG)	German Society (if do not differ from patient valuation)	French societal preferences	Australian (or similar) societal preferences
Preferred method for valuing health states	Choice-based method (TTO/SG)	Not specified	Not specified	Consistent approach (TTO/SG/VAS)	French value set (approach) - whichever prevails	Not sp

Abbreviations: CADTH, Canadian Agency for Drugs and Technologies in Health; HAS, Haute Autorité de Santé; HTA, health technology assessment; HRQoL, health-related quality of life; ICER, Institute fo Review; IQWiG, Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen [Institute for Quality and Efficiency in Health Care]; NICE, National Institute for Health and Care Excellence; GPBM, Generic pr standard gamble; TTO, time trade-off. **Note:** * mapping function by van Hout et al. (2012) to EQ-5D-3L recommended.

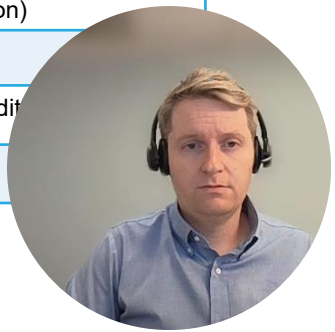
1. NICE health technology evaluations: the manual. 2022. https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation
2. CADTH (4th Edition). Guidelines for the Economic Evaluation of Health Technologies. https://www.cadth.ca/guidelines-economic-evaluation-health-technologies-canada-0
3. ICER Value Assessment Framework, 2023. https://icer.org/wp-content/uploads/2023/09/ICER_2023_VAF_For-Publication_092523.pdf
4. IQWIG, 2023. General Methods 7.0. https://www.iqwig.de/methoden/general-methods_version-7-0.pdf
5. HAS, 2020. https://www.has-sante.fr/upload/docs/application/pdf/2020-11/methodological_guidance_2020_-choices_in_methods_for_economic_evaluation.pdf



Types of RWD Studies to Inform HTA

	Purposes of RWD collection	Pre-licence	Post-licence
	Describing current Tx patterns for a patient group for baseline information	✓	✓
1.	Measuring healthcare-related resource use and burden-of-illness	✓ (if disease-related)	✓ (if related to new intervention)
	Evaluating prescribing patterns of the new medicine		✓
2.	Evaluating clinical outcomes associated with the new Tx (e.g. durability)		✓ (comparative or non-comparative)
3.	Collecting quality of life data for economic modelling	✓ (if disease-state based)	✓
4.	Patient experience or PROs in real clinical practice	✓ (baseline information on current management)	✓ (if related to new intervention)
	Evaluating service delivery and the impact of service improvement activities	✓	✓
	Collecting patient safety data on the use of the new Tx		✓ (or condit
	Understanding patient profiles in the disease area	✓	✓

Note: Table adapted from Association of the British Pharmaceutical Industry (ABPI) 'Vision for RWD' report, 2011. https://www.abpi.org.uk/media/pvzfhi1p/vision-for-real-world-data.pdf



HTA, Health Technology Assessment; PRO, Patient-Reported Outcomes; PRW, Prospective Real-World; RWD, Real World Data; Tx, Treatment.

1. Measuring Healthcare-Related Resource Use and Burden-of-Illness in Single Technology Appraisals

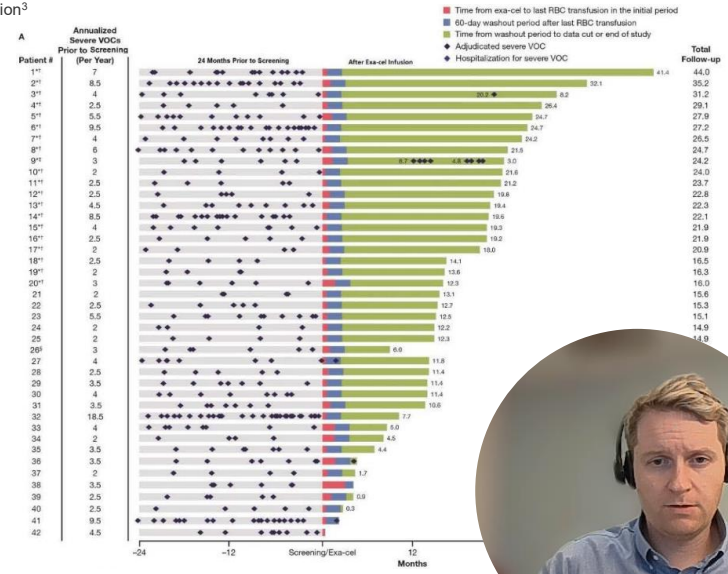
Challenge:

- Exagamglogene autotemcel (Casgevy) presents a gene-editing therapy (GTx) for sickle cell disease (SCD) in ≥12 years, with recurrent vaso-occlusive crises (VOCs).
  - Single-arm trials (CLIMB SCD-121 and 131).
- Few studies have used validated generic and SCD-specific PRO instruments.

Approach:

- PRW PRO study conducted to contextualize findings from single-arm trials. [1,2]
  - Inform humanistic and economic burden.
  - Confirm sustained burden over time.
    - Worse scores across FACT-G domains compared to population norms.
    - FACIT-F scores worse than patients with anemic cancer.

Figure 1. Duration of Period Free from VOCs (Study CLIMB SCD-121 and Study 121) after Exa-cel Infusion[3]



Note: A
(2024).[3]

Takeaway: PRW PRO data collection routinely included in regulatory submissions for NICE (and other HTA bodies).

FACT-G, Functional Assessment of Cancer Therapy-General; FACT-F, Functional Assessment of Cancer Therapy-Fatigue; GTx, Gene-editing Therapy; MAA, Managed Access Agreement; PRW, Prospective Real World Study; PRO, Patient-Reported Outcomes; SCD, Sickle Cell Disease; VOCs, Vaso-Occlusive Crises.

1. NICE, 2024. https://www.nice.org.uk/guidance/gid-ta11249/documents/committee-papers
2. Drahos, 2022. https://doi.org/10.1182/blood-2022-157818
3. Frangoul, 2024. https://www.nejm.org/doi/10.1056/NEJMoa2309676

2. Evaluating Clinical Outcomes associated with the New Treatments via Cancer Drugs Fund

- NICE decisions include:
  - **Recommended / Not Recommended**
  - **Optimized** - Tx available for certain people with a condition.
  - **Only in research** -Tx available as part of trial/study.
  - **Recommended for use within the Cancer Drug Fund (CDF)**
- NHS England and NICE partner with companies to address uncertainty.
- Data Collection Agreement (DCA) within managed access agreements (MAA).

- Trastuzumab deruxtecan (Enhertu) treats HER2+ unresectable or metastatic breast cancer after 1 or more anti-HER2 therapies (TA862).
  - DCA as continuation of trial and RWD collection from the National Disease Registration Service.
    - DESTINY-Breast03 is a phase 3, multi-center, open-label randomized trial.
    - HRQoL included as secondary endpoint (EQ-5D-5L, EORTC QLQ-C30, and EORTC QLQ-BR45).
  - RWD via NHS Digital (SACT and Blueteq system).

Figure 1. Positive cancer appraisal recommendations pre/post CDF re-launch (2016)

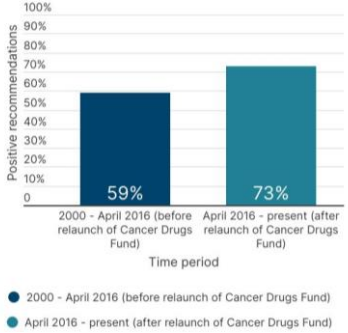


Figure 2. Technology appraisal data: cancer appraisal recommenda

Takeaway: RWD follow-up is routine but limited PRW PRO data collection of outside of trials via CDF (and MAAs).

CDA, Cancer Drugs Fund; MAA, Managed Access Agreement; NICE, National Institute for Health and Care Excellence; NHS, National Health Service; PROs, Patient-Reported Outcomes; RWD, Real World Data; SACT, Systemic Anti-Cancer Therapy (Dataset); Tx, Treatments.

NICE, 2022. https://www.nice.org.uk/guidance/ta862/resources/managed-access-agreement-pdf-11373006493

3. Collecting Quality of Life Data for Economic Modelling

Challenge:

- Nusinersen (Spinraza) was developed to spinal muscular atrophy (SMA), an inherited neuromuscular disorder.
- Trial data shows that Spinraza improves clinical outcomes in early (type 1) and later onset (types 2 and 3) SMA.
  - Some evidence suggesting that Tx effective for pre-symptomatic SMA.
- NICE highlighted limited long-term evidence and uncertainty (in HRQoL inputs).

Approach:

- MAA ongoing with SMA Patient Registries.[1]
  - DCA as per the MAA will be entered by clinicians into the SMA REACH UK and Adult SMA REACH registries.
- Follow-up of Patient and Carer HRQoL to inform economic modelling.
  - People who have lost the ability to walk but have received Spinraza report improvements in daily activities.
- Review of the guidance by the end of the fifth year (Due: 2024/25).

Figure 1. Nusinersen for treating SMA

Marketing authorisation indication	Nusinersen (Spinraza, Biogen Idec) has a marketing authorisation for 'the treatment of 5q spinal muscular atrophy'.
Dosage in the marketing authorisation	12 mg, by intrathecal infusion, on days 0, 14, 28 and 63, then every 4 months.
Price	The list price is £75,000 per vial (excluding VAT; BNF, accessed June 2018) At the list price, the total annual treatment cost is £450,000 for the first year and £225,000 for subsequent years. Over 5 years, the treatment costs per person would be £1.35 million. The company has a commercial arrangement. This makes nusinersen available to the NHS with a discount. The size of the discount is commercial in confidence. It is the company's responsibility to let relevant NHS organisations know details of the discount.

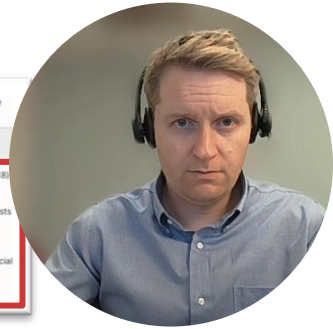


Table 1. Classification and Subtypes of SMA

Type	Age of onset	Max. motor milestone	Motor ability and additional features	Survival
T0	Before birth	None	Severe hypotonia; unable to sit and roll	Respiratory insufficiency at birth: death within weeks
T1	2 weeks (Ia) 3 months (Ib) 6 months (Ic)	None	Severe hypotonia; unable to sit and roll	Death/ventilation by 2 years
T2	6–18 months	Sitting	Proximal weakness: unable to walk independently	Survival into adulthood (typically >25 years)
T3	<3 years (IIIa) >3 years (IIIb) >12 years (IIIc)	Walking	May lose ability to walk	Normal life span
T4	>30 years or 10–30 years	Normal	Mild motor impairment	Normal life span

Takeaway: PRW PRO studies are routinely conducted to address uncertainties in economic modelling.

HRQoL, Health-Related Quality of Life; MAA, Managed Access Agreement; SMA, Spinal Muscular Atrophy.

1. NICE, 2019. https://www.nice.org.uk/guidance/ta588/resources

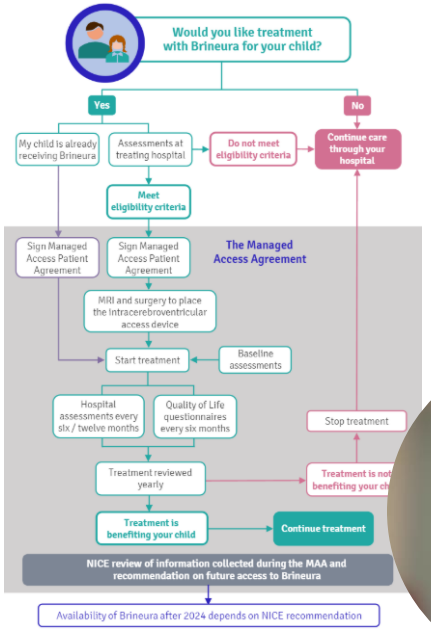
4. Patient Experience or Patient-reported Outcomes in real Clinical Practice via MAAs

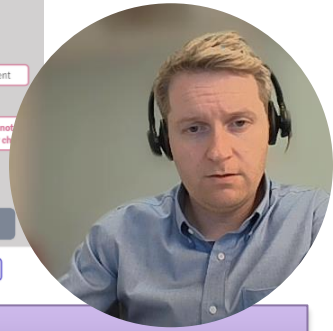
- Neuronal Ceroid Lipofuscinosis Type 2 (CLN2) (or Batten Disease) is a rare neurodegenerative genetic disease that affects children from early life.
  - Progressive, leading to early death in childhood.
- Cerliponase alfa (Brineura) developed to treat CLN2.

- NICE committee considered some key uncertainties were:
  - Long-term disease stabilization; and
  - Improvements in Motor and Language (ML) score.
  - and **measures of quality of life**.

- A MAA with DCA to collect data from all patients who receive treatment. Two data collection streams:
  - 1) Clinical data collected by the treating clinician, including clinical, safety and efficacy data.
  - 2) PRO data collected (by a third party) including PedsQL, CLN2QoL, and EQ-5D-5L (completed by telephone every 6 months) – considering child and family/caregiver QoL.

Figure 1. Simplified overview of MAA for Brineura





Takeaway: PRW PRO studies are conducted to describe patient experience in clinical practice.

CLN2, Neuronal Ceroid Lipofuscinosis Type 2; DCA, Data Collection Agreement; MAA, Managed Access Agreement; NICE, National Institute for Health and Care Excellence; NHS, National Health Service; PROs, Patient-Reported Outcomes; RWD, Real World Data; Tx, Treatments.

NICE, 2023. https://www.nice.org.uk/guidance/hst12/resources/managed-access-agreement-pdf-6968825245

Summary

- Different types of PRW PRO data ‘can’ and ‘are’ influencing decision-making.

- RCTs are preferred source of evidence but growing appreciation of challenges.
  - RCT evidence not always sufficient/appropriate.
  - Single arm trials are increasingly common.

- HTA bodies value the patient perspective.
  - GPBM with good psychometric performance are preferred.
  - Consider alternative approaches and ‘hierarchy of evidence’.

- A pragmatic approach is often necessary in the context of many unknowns (and unmet needs) in rare disease.
  - Alternative data sources (including PRW PRO data) can reduce uncertainty in HTA decision-making.

GPBM, Generic Preference-Based Measures; HTA, Health Technology Assessment; PRO, Patient Reported Outcomes; PRW, Prospective Real World; RCT, Randomized Controlled Trials; RWD, Real World Data; Tx, Treatment.

SECTION

6

Audience Participation

Are there any other aspects/issues that should be addressed by the TF recommendations?

What challenges do you experience when conducting RW studies gathering PRO data?

Do you have working examples/case studies where PRO data from RW studies have made a difference to your work outputs?

How AI will impact the way the RWE studies are conducted?

Related ISPOR Activities

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- **Clinical Outcomes Assessment (COA) SIG**
- **Patient Centered SIG**
- **RWE SIG**


thank you
danke
謝謝
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teşekkür ederim
gracias
merci
obrigado
dziękuję
bedankt
go raibh maith agat
mochchakkeram
dank je
спасибо
Баярлалаа
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tapadh leat
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