Advancing Tolerability Assessment Through Real-World Patient-Reported Outcomes (RW-PROs)

PSI 2026 Conference
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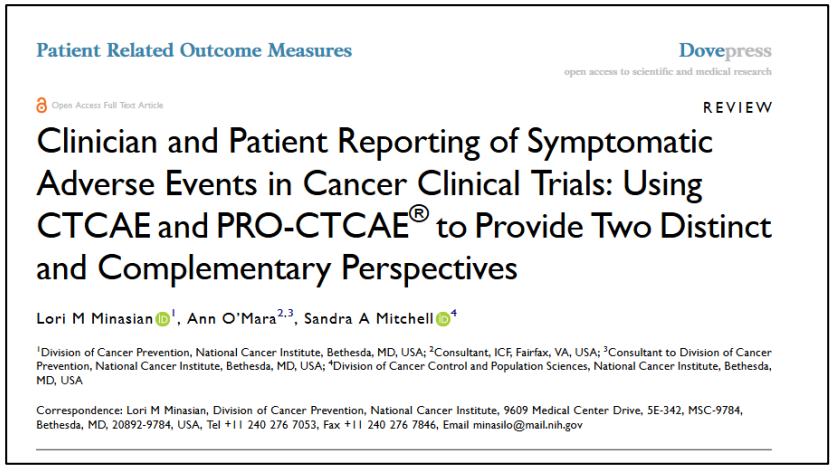
PROs for assessing tolerability

Safety

- Safety measures the medical and biological risks to the subject.
- PROs are already widely used to assess the safety of health interventions.
- Evidence suggests that healthcare professionals and patients often report adverse events differently.



Patient Related Outcome Measures

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REVIEW

Clinician and Patient Reporting of Symptomatic Adverse Events in Cancer Clinical Trials: Using CTCAE and PRO-CTCAE® to Provide Two Distinct and Complementary Perspectives

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Tolerability

- Tolerability reflects the degree to which treatment-related adverse effects are acceptable and manageable for a patient.
- Asking patients is the most straightforward and appropriate way to assess tolerability.

Direct patient reporting of tolerability has gained considerable attention in recent years, is now widely used in oncology trials, and is expected to play an increasingly important role in other clinical settings.

PROs for assessing tolerability

- The value of direct patient reporting of tolerability has been recognised by the FDA.
- Measurement of overall tolerability is recommended within the core PRO set for oncology trials.

GP5 (Version 4)

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

		Not at all	A little bit	Somewhat	Quite a bit	Very much
GP5	I am bothered by side effects of treatment.....	0	1	2	3	4

EORTC item Q168

To what extent have you been troubled with side effects from your treatment?

Not at all A little Quite a bit Very much

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Core Patient-Reported Outcomes in Cancer Clinical Trials

Guidance for Industry

FDA U.S. FOOD & DRUG ADMINISTRATION

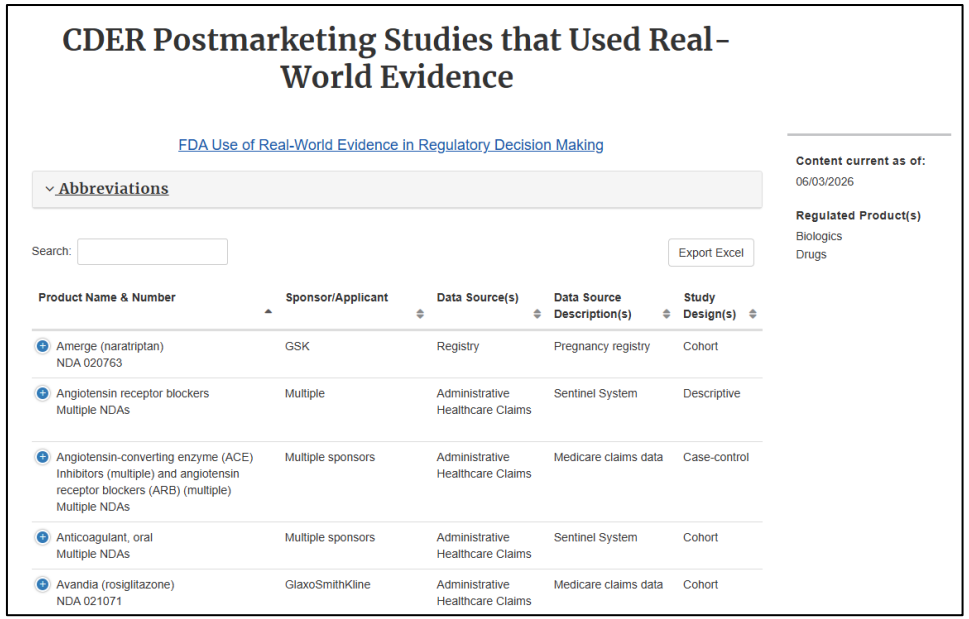
U.S. Department of Health and Human Services
Food and Drug Administration
Oncology Center of Excellence (OCE)
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)

October 2024
Clinical/Medical

Real-World PROs (RW-PROs)

- Real-world evidence (RWE) can be generated prospectively or retrospectively using diverse study designs.
- While typically associated with post-approval research, RWE can also be generated in certain pre-approval settings.
- RWE is attracting increasing attention from both payers and regulators.

PROs play a central role in advancing patient-centricity in RWE generation.



CDER Postmarketing Studies that Used Real-World Evidence

FDA Use of Real-World Evidence in Regulatory Decision Making

Abbreviations

Search: Export Excel

Product Name & Number	Sponsor/Applicant	Data Source(s)	Data Source Description(s)	Study Design(s)
Amerge (naratriptan) NDA 020763	GSK	Registry	Pregnancy registry	Cohort
Angiotensin receptor blockers Multiple NDAs	Multiple	Administrative Healthcare Claims	Sentinel System	Descriptive
Angiotensin-converting enzyme (ACE) Inhibitors (multiple) and angiotensin receptor blockers (ARB) (multiple) Multiple NDAs	Multiple sponsors	Administrative Healthcare Claims	Medicare claims data	Case-control
Anticoagulant, oral Multiple NDAs	Multiple sponsors	Administrative Healthcare Claims	Sentinel System	Cohort
Avandia (rosiglitazone) NDA 021071	GlaxoSmithKline	Administrative Healthcare Claims	Medicare claims data	Cohort

Content current as of: 06/03/2026

Regulated Product(s): Biologics, Drugs

Source: https://www.fda.gov/science-research/real-world-evidence/fda-use-real-world-evidence-regulatory-decision-making

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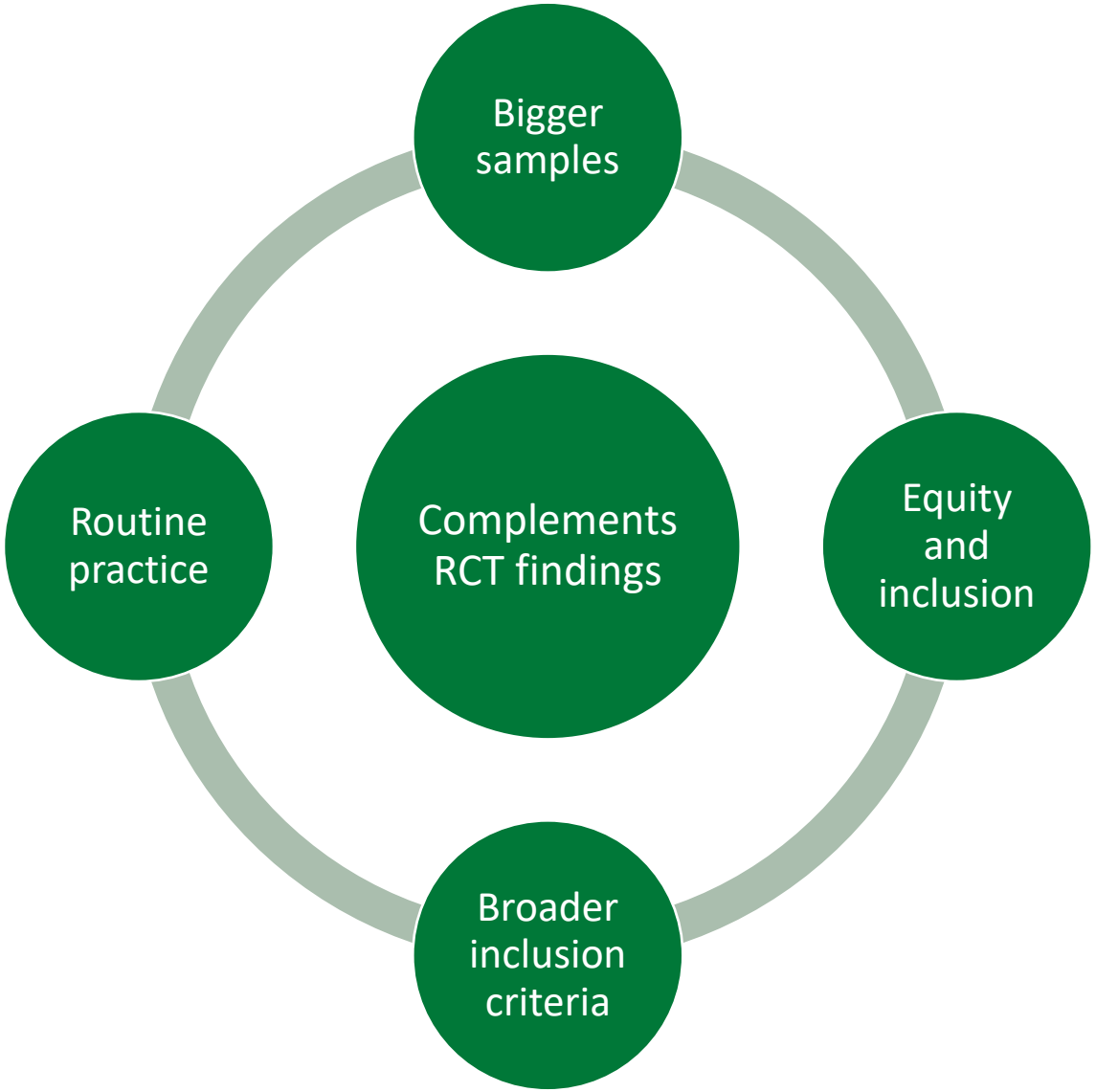
Value of RW-PROs

RW-PROs are particularly valuable for long-term follow-up, where safety and tolerability are key considerations.



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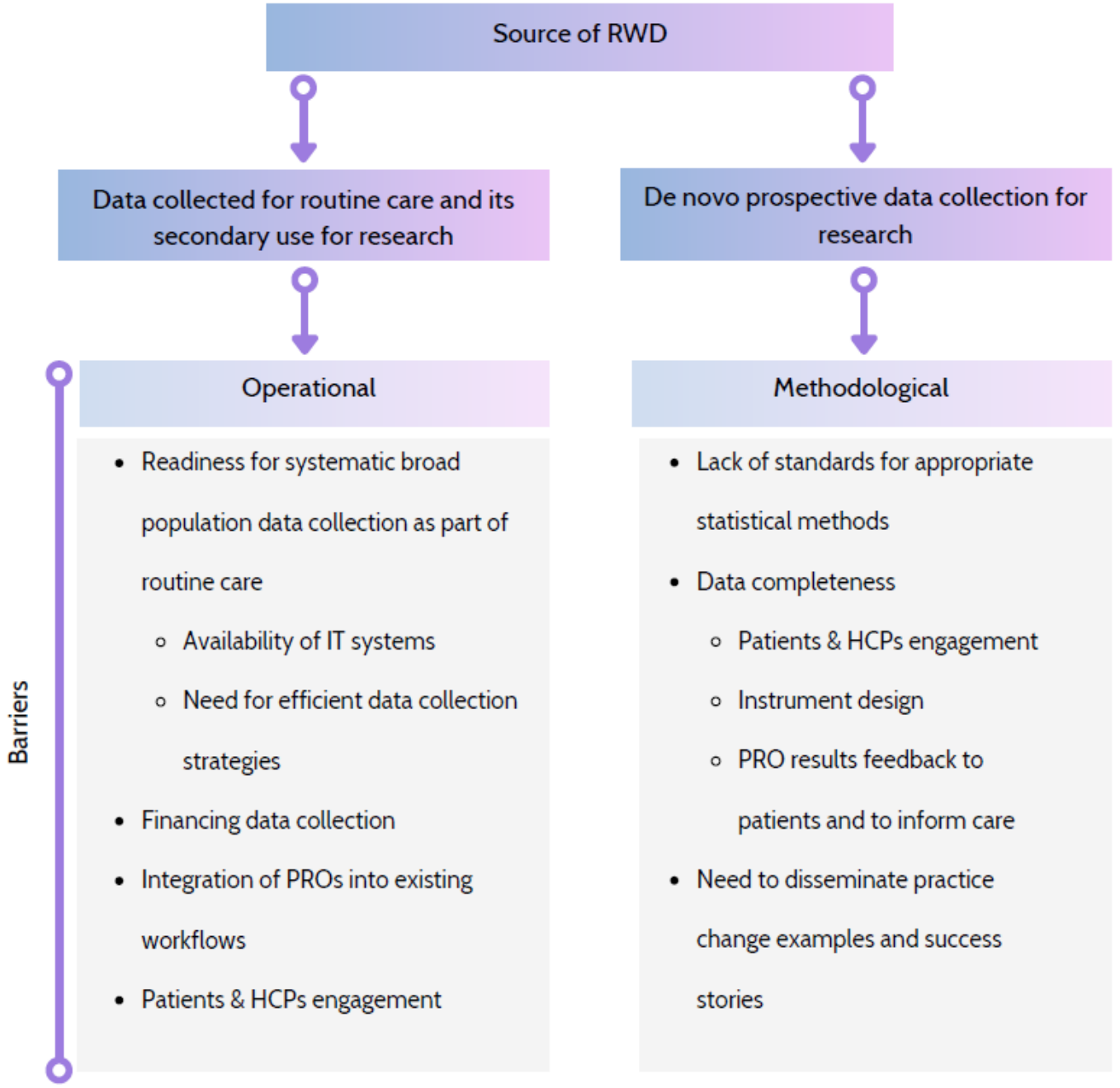
Existing barriers

Missing data are a major concern



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Source: Maruszczyk 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 Sep 14;9(9):e20157. doi: 10.1016/j.heliyon.2023.e20157.

Useful resources

- PRO guidance (clinical trials & routine practice)
- RWE guidance
- Emerging RW-PRO-specific recommendations

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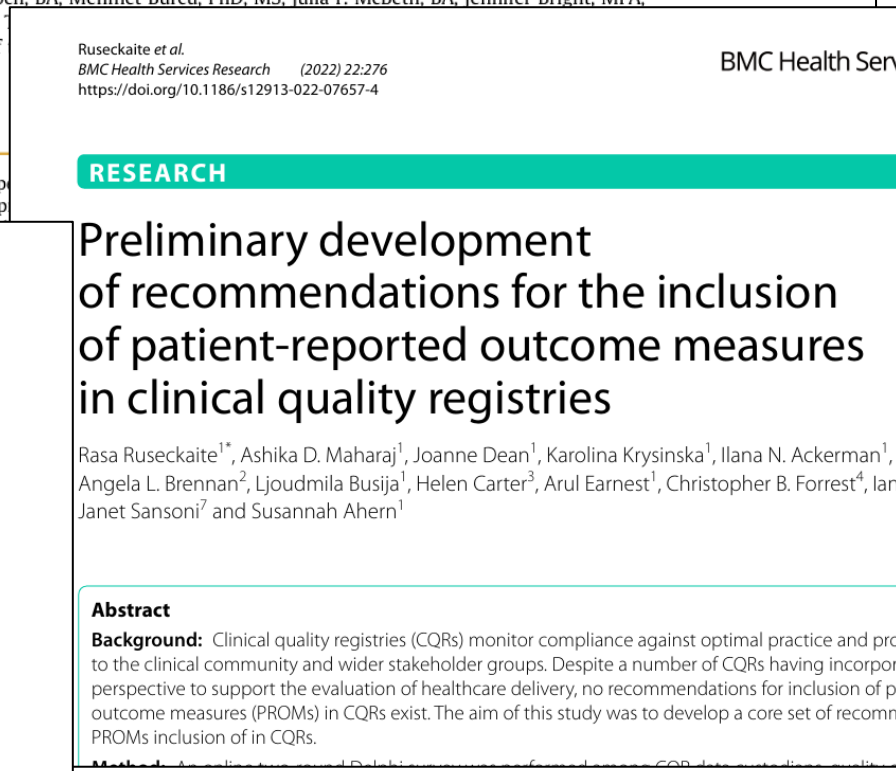
Themed Section: The Patient Journey

Developing Patient-Centered Real-World Evidence: Emerging Methods Recommendations From a Consensus Process

Elisabeth M. Oehrlein, PhD, MS, Silke Schoch, BA, Mehmet Burcu, PhD, MS, Julia F. McBeth, BA, Jennifer Bright, MPA, Chris L. Pashos, PhD, Richard Willke, PhD, Eleanor M. Perfetto, PhD, MS, on behalf of

ABSTRACT

Objectives: The Joint ISPOR-ISPE Sp
recommended good procedural p



Ruseckaite *et al.*
BMC Health Services Research (2022) 22:276
https://doi.org/10.1186/s12913-022-07657-4

BMC Health Serv

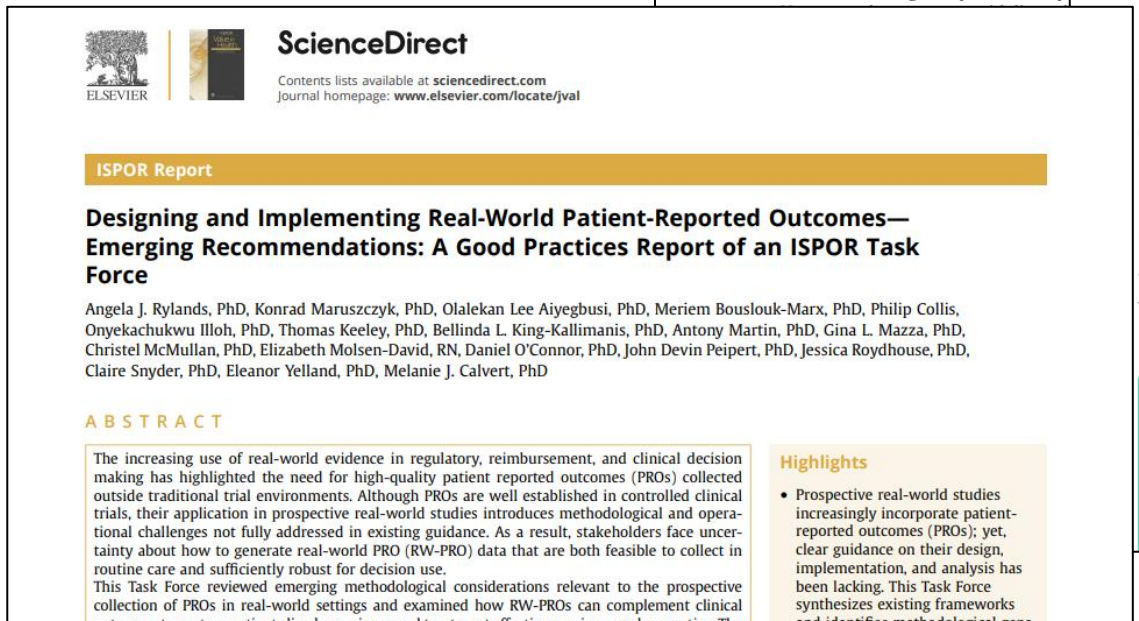
RESEARCH

Preliminary development of recommendations for the inclusion of patient-reported outcome measures in clinical quality registries

Rasa Ruseckaite[1*], Ashika D. Maharaj[1], Joanne Dean[1], Karolina Krysinska[1], Ilana N. Ackerman[1], Angela L. Brennan[2], Ljoudmila Busija[1], Helen Carter[3], Arul Earnest[1], Christopher B. Forrest[4], Ian Janet Sansoni[7] and Susannah Ahern[1]

Abstract

Background: Clinical quality registries (CQRs) monitor compliance against optimal practice and pro to the clinical community and wider stakeholder groups. Despite a number of CQRs having incorpor perspective to support the evaluation of healthcare delivery, no recommendations for inclusion of p outcome measures (PROMs) in CQRs exist. The aim of this study was to develop a core set of recomm PROMs inclusion of in CQRs.



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ISPOR Report

Designing and Implementing Real-World Patient-Reported Outcomes—Emerging Recommendations: A Good Practices Report of an ISPOR Task Force

Angela J. Rylands, PhD, Konrad Maruszczyk, PhD, Olalekan Lee Aiyegbusi, PhD, Meriem Bouslouk-Marx, PhD, Philip Collis, Onyekachukwu Illoh, PhD, Thomas Keeley, PhD, Bellinda L. King-Kallimanis, PhD, Antony Martin, PhD, Gina L. Mazza, PhD, Christel McMullan, PhD, Elizabeth Molsen-David, RN, Daniel O'Connor, PhD, John Devin Peipert, PhD, Jessica Roydhouse, PhD, Claire Snyder, PhD, Eleanor Yelland, PhD, Melanie J. Calvert, PhD

ABSTRACT

The increasing use of real-world evidence in regulatory, reimbursement, and clinical decision making has highlighted the need for high-quality patient reported outcomes (PROs) collected outside traditional trial environments. Although PROs are well established in controlled clinical trials, their application in prospective real-world studies introduces methodological and operational challenges not fully addressed in existing guidance. As a result, stakeholders face uncertainty about how to generate real-world PRO (RW-PRO) data that are both feasible to collect in routine care and sufficiently robust for decision use.
This Task Force reviewed emerging methodological considerations relevant to the prospective collection of PROs in real-world settings and examined how RW-PROs can complement clinical

Highlights

- Prospective real-world studies increasingly incorporate patient-reported outcomes (PROs); yet, clear guidance on their design, implementation, and analysis has been lacking. This Task Force synthesizes existing frameworks

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ISPOR Task Force on prospective RW-PROs

Source: Rylands et al. Designing and Implementing Real-World Patient-Reported Outcomes-Emerging Recommendations: A Good Practices Report of an ISPOR Task Force. *Value Health.* 2026 Mar 18:S1098-3015(26)00102-6. doi: 10.1016/j.jval.2026.02.018.

Tolerability of Advanced Therapies

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Centre of Excellence in Regulatory Science and Innovation for Advanced Therapies

Advanced therapy medicinal products (ATMPs)

Play an increasingly important role in the treatment of burdensome and complex diseases

- Especially used for treatment of rare diseases

Many ATMPs offer the potential for significant, life-changing benefits to patients

- Some have curative or pseudo-curative potential

Safety and tolerability profiles are not always fully understood

- Short-term
- **Long-term**

It is critical that regulatory evaluation of ATMPs includes consideration of the patient experience

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Tolerability of Advanced Therapies

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Review of regulatory guidance

ICH
harmonisation for better health

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

FDA U.S. FOOD & DRUG ADMINISTRATION

- PROs recognised as acceptable evidence for regulatory decision-making
- No ATMP-specific guidance currently available for PRO assessment

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Tolerability of Advanced Therapies

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Case studies

Drug	Casgevy	Hemgenix
Indication	SCD and TDT	Haemophilia B
PROs used to characterise disease burden	✓	✓
Interim PRO findings demonstrated favourable outcomes	✓	
Final assessment pending trial completion	✓	
PRO data used to derive health-state utilities for economic models	✓	✓
RW-PRO results used to contextualise broader quality-of-life outcomes	✓	
PROs incorporated into long-term post-authorisation RWE studies	✓	✓

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Tolerability of Advanced Therapies

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Main findings

- Widespread recognition of the importance of PROs in the evaluation of ATMPs
- Specific guidance may help further optimise their use
  - Methodological advancement in PRO use in small, single-arm design will further support regulatory decision-making
- RW-PROs from long-term follow-up may help demonstrate broader patient benefits

Next steps

- Develop a Framework for Patient-Centred Outcomes for Individualised Genetic Therapies
- Feasibility and Initial Plans for Regulatory Monitoring of ATMP Safety Using PROs

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Key Considerations for the Use of RW-PROs in Tolerability Assessment

- Selection of most appropriate PRO measures
- Determine PRO assessment timing and frequency
- Plan for verifying data provenance
- Plan for handling data missingness
- Field test of data capture approaches

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Summary

- Patient-centricity is critical in the evaluation of tolerability of new treatments in RW settings.

- RW-PRO can provide valuable insights into the burden of disease, long-term tolerability and effectiveness in more generalisable populations.

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Thank you!

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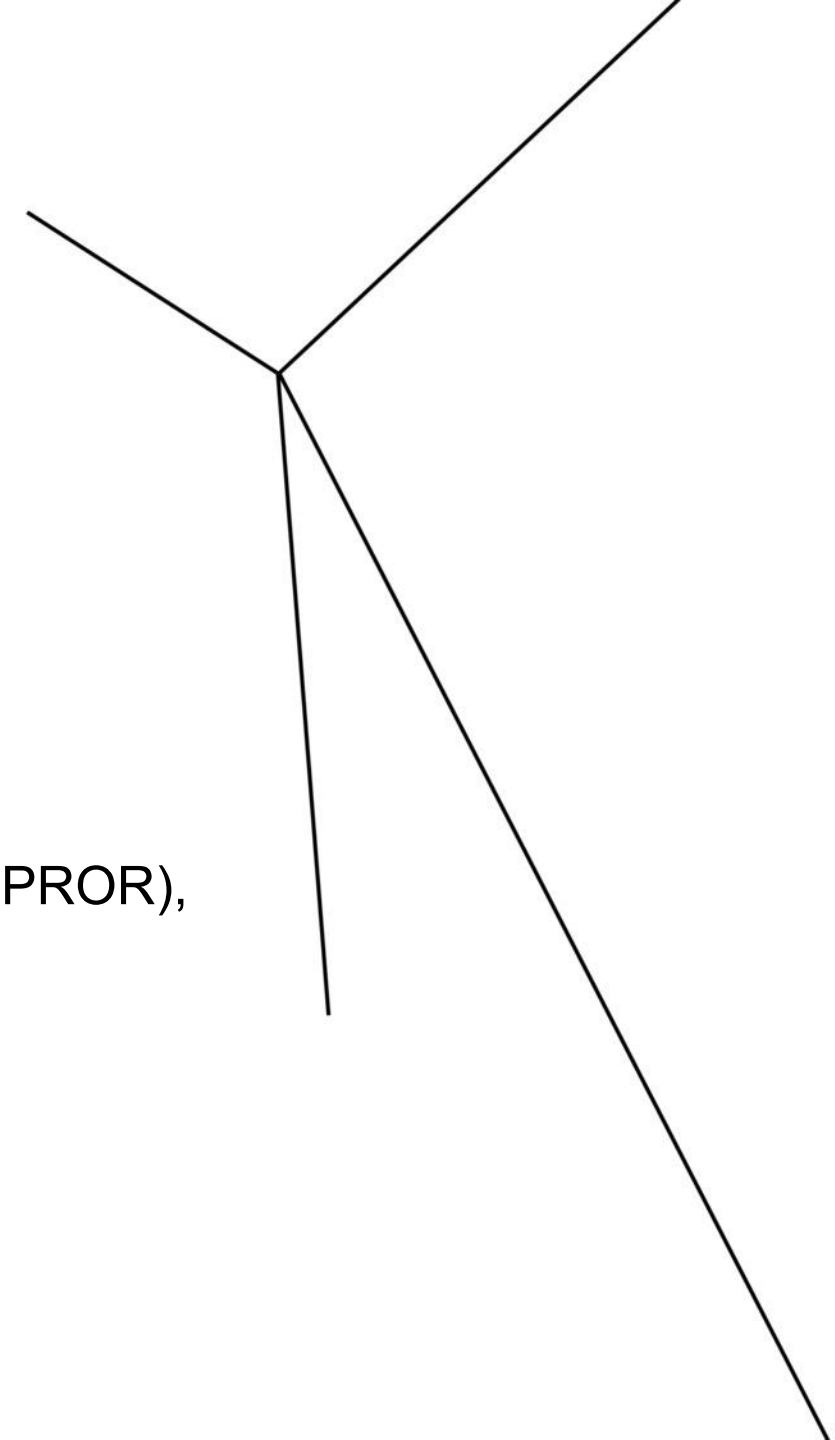

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