Reporting the PRO Results Clearly - Part 1
The CONSORT PRO Extension

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Funded by the Patient-Centered Outcomes Research Institute and Genentech

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Patient-Reported Outcomes Tools: Engaging Users and Stakeholders

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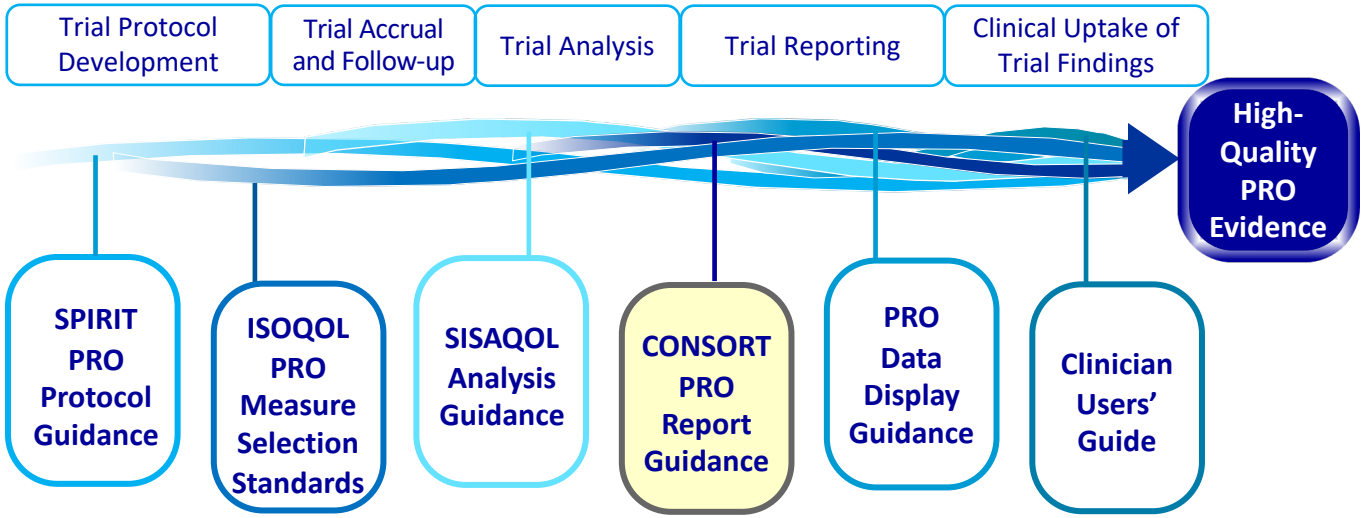
Overview of Presentations

Introduction to PROs and PROTEUS

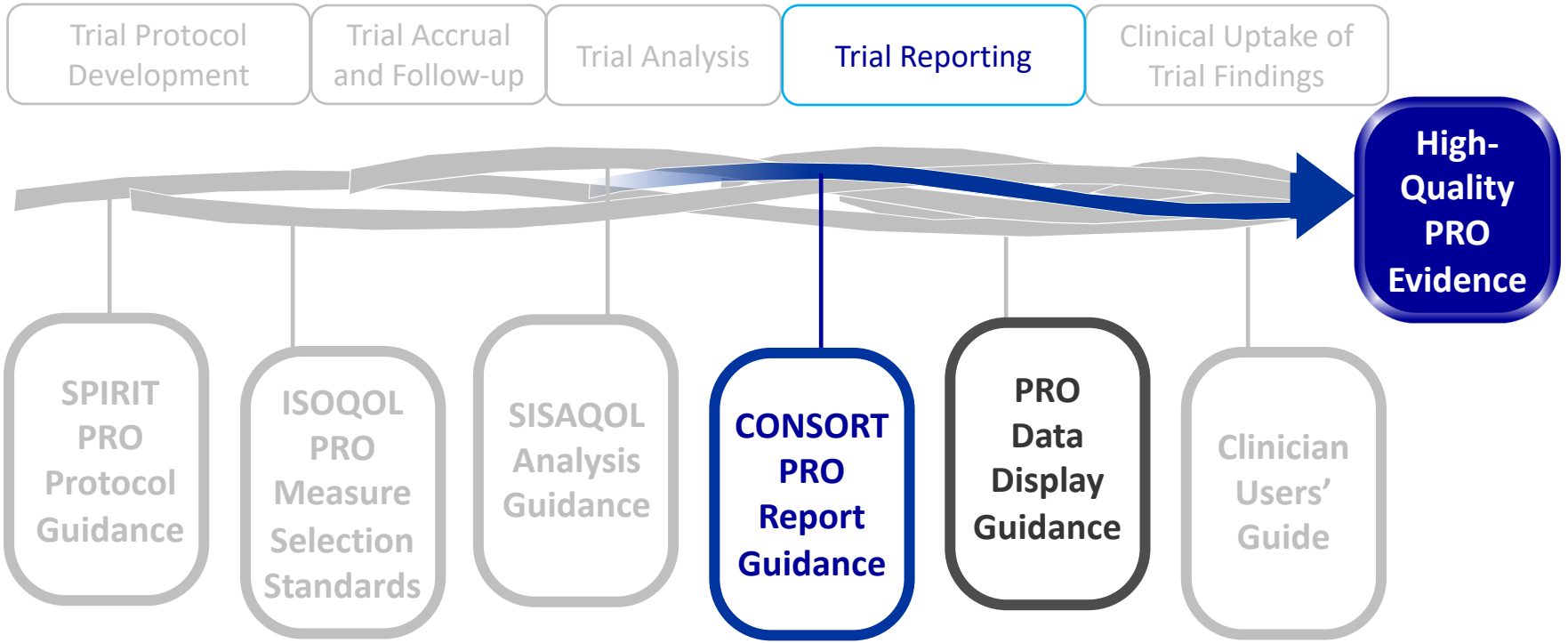
Introduction to the PROTEUS Tools



→ Overview of Tool Recommendations

→ How to Apply the Tools

Reporting the PRO Results Clearly (1)



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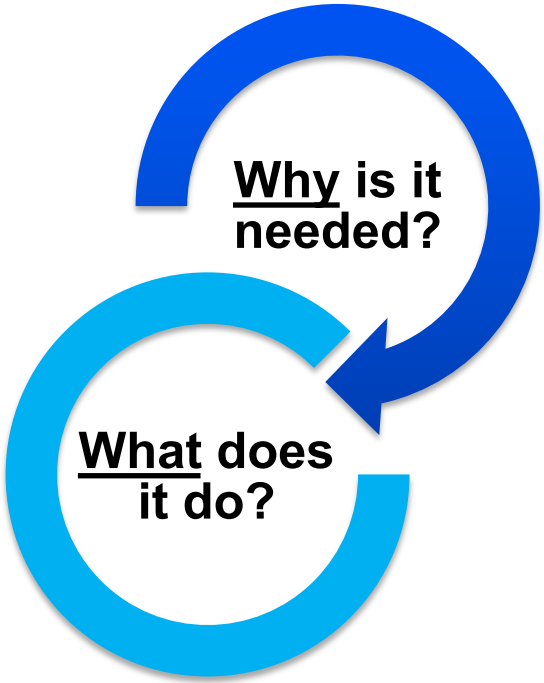
Reporting PRO Results Clearly – Part 1



To ensure that the PRO methods and results are clearly described in clinical trial publications

Identifies the relevant information to include in clinical trial publications with PRO endpoints

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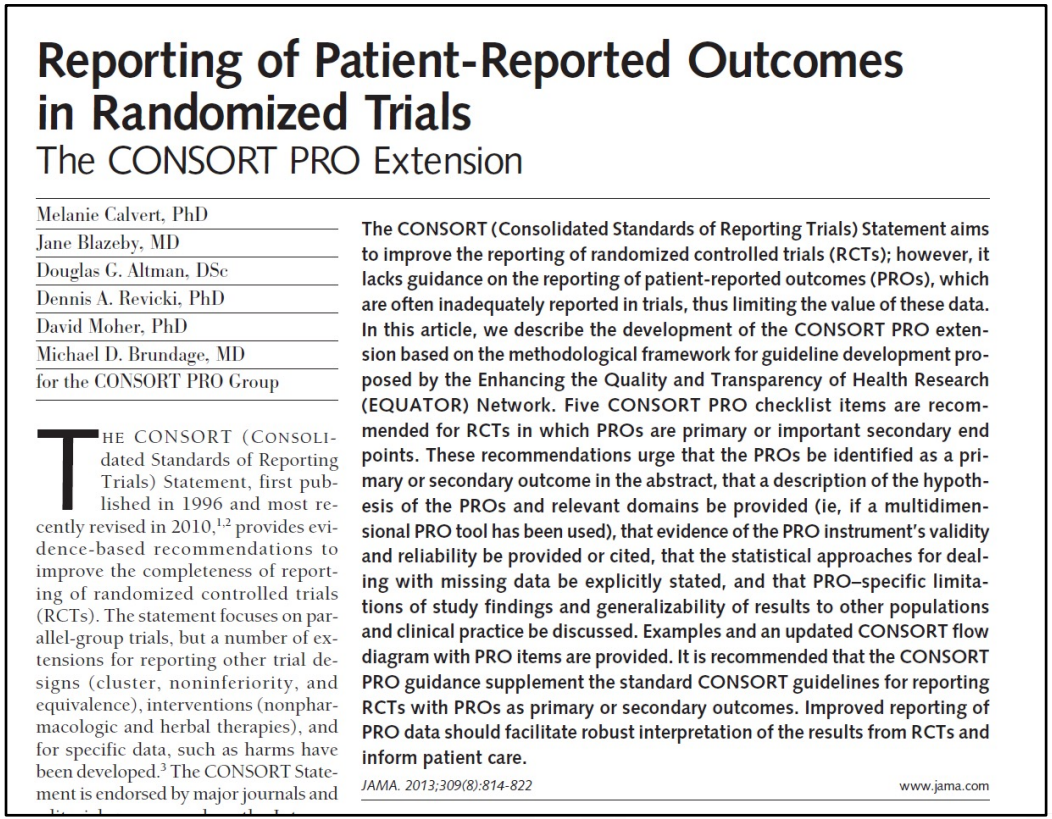
Reporting the PRO Results Clearly (1)



Reporting of Patient-Reported Outcomes in Randomized Trials

The CONSORT PRO Extension

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The CONSORT (Consolidated Standards of Reporting Trials) Statement aims to improve the reporting of randomized controlled trials (RCTs); however, it lacks guidance on the reporting of patient-reported outcomes (PROs), which are often inadequately reported in trials, thus limiting the value of these data. In this article, we describe the development of the CONSORT PRO extension based on the methodological framework for guideline development proposed by the Enhancing the Quality and Transparency of Health Research (EQUATOR) Network. Five CONSORT PRO checklist items are recommended for RCTs in which PROs are primary or important secondary end points. These recommendations urge that the PROs be identified as a primary or secondary outcome in the abstract, that a description of the hypothesis of the PROs and relevant domains be provided (ie, if a multidimensional PRO tool has been used), that evidence of the PRO instrument's validity and reliability be provided or cited, that the statistical approaches for dealing with missing data be explicitly stated, and that PRO–specific limitations of study findings and generalizability of results to other populations and clinical practice be discussed. Examples and an updated CONSORT flow diagram with PRO items are provided. It is recommended that the CONSORT PRO guidance supplement the standard CONSORT guidelines for reporting RCTs with PROs as primary or secondary outcomes. Improved reporting of PRO data should facilitate robust interpretation of the results from RCTs and inform patient care.

JAMA. 2013;309(8):814-822 www.jama.com

THE CONSORT (Consolidated Standards of Reporting Trials) Statement, first published in 1996 and most recently revised in 2010,[1,2] provides evidence-based recommendations to improve the completeness of reporting of randomized controlled trials (RCTs). The statement focuses on parallel-group trials, but a number of extensions for reporting other trial designs (cluster, noninferiority, and equivalence), interventions (nonpharmacologic and herbal therapies), and for specific data, such as harms have been developed.[3] The CONSORT Statement is endorsed by major journals and

Calvert et al, JAMA 2013, 309(8), 814-822

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CONSORT Executive & EQUATOR Network

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University of Birmingham, UK, Queens University, Canada, University of Bristol, UK, University of Ottawa, Canada, University of Oxford, UK, United BioSource Corporation, Bethesda, MD, USA

Survey participants including: ISPOR, MRC HTMR, NIHR Research design service, SCT, European Clinical Trials Units, Journal Editors, Policy Makers

Meeting participants

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Why We Need PRO Reporting Guidance

- Clinicians, patients and policy makers value PRO information
- Existing reporting guidelines are not adhered to
- Poor reporting hampers the use of PRO data in clinical practice and undermines the clinicians' ability to use PRO data in their practice to benefit patients
- Improved reporting of PRO data should facilitate robust interpretation of the results from RCTs and inform patient care

Brundage et al, Qual Life Res 2011, 20(5), 653-664
Brundage et al, Qual Life Res 2012, 22(6), 1161-75

Objective of Resource

- The CONSORT (Consolidated Standards of Reporting Trials) Statement aims to improve the reporting of randomized controlled trials (RCTs), however lacks guidance on the reporting of PROs

- Provide an evidence-based extension of the CONSORT statement for reporting PROs in RCTs (extensions) and to elaborate on the CONSORT 2010 statement specifically as applied to PROs (elaborations)

Overview of CONSORT-PRO Reporting Guidance

- To be used in conjunction with the CONSORT 2010 Statement and related extensions appropriate for the trial design
- 5 additional checklist items (extensions) recommended to be reported in all RCTs where PROs are a primary or important secondary outcome
- Provides additional elaboration on the existing CONSORT 2010 checklist items as applied to the reporting of PROs in RCTs

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PRO Extension – Abstract Item 1b

CONSORT 2010:

Structured summary of trial design, methods, results, and conclusions.

PRO Extension 2013:

The PRO should be identified in the abstract as a primary or secondary outcome.

Explanation:

Will facilitate indexing and identification of studies to inform clinical care and evidence synthesis.

PRO Extension – Introduction Item 2b

CONSORT 2010:

Specific objectives or hypotheses.

PRO Extension 2013:

The PRO hypothesis should be stated and relevant domains identified, if applicable.

Explanation:

Without a prespecified hypothesis there is risk of multiple statistical testing and selective reporting of significant results.

PRO Extension – Methods Item 6a

CONSORT 2010:

Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.

PRO Extension 2013:

Evidence of PRO instrument validity and reliability should be provided or cited, if available.

Explanation:

Clinical use of PRO data requires that the trial results are robust, which depends on a valid and reliable PRO measure being used appropriately.

PRO Extension – Methods Item 12a

CONSORT 2010:

Statistical methods used to compare groups for primary and secondary outcomes.

PRO Extension 2013:

Statistical approaches for dealing with missing data should be explicitly stated.

Explanation:

The level of missing PRO data is often high and can lead to reduced power, is a potential source of bias, and can result in misleading results.

PRO Extension – Discussion Item 20/21

CONSORT 2010:

Item 20. Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses.

Item 21. Generalizability (external validity, applicability) of the trial findings.

PRO Extension 2013:

PRO specific limitations and implications for generalizability of study findings and clinical practice.

Explanation:

Readers need to be able to assess generalizability and any potential sources of bias.

PRO Elaborations

PRO Elaboration – Introduction Item 2a

CONSORT 2010:

Scientific background and explanation of rationale.

PRO Extension 2013:

The relevant background and rationale for why PROs were assessed in the RCT should be briefly described.

Explanation:

The Background or Methods section should provide the rationale for including PROs and why the specific outcomes were selected, thus providing appropriate context for the PRO-specific objectives and hypotheses.

PRO Elaboration – Methods Item 6a

CONSORT 2010:

Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed.

PRO Extension 2013:

Details of the mode of PRO completion (in particular if a proxy completed the question-naire on behalf of the patient), and the method of data collection (paper, tele-phone, electronic, other) should also ideally be provided particularly when the PRO is the primary outcome.

Explanation:

Different methods of data collection may affect the results and lead to potential bias if used differentially between intervention groups.

PRO Elaboration – Results Item 13a

CONSORT 2010:

For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome.

PRO Extension 2013:

The number of participants reporting PRO data at baseline and at subsequent time points should be made transparent.

Explanation:

The flow of participants through the trial in relation to PROs, including information on the reason for missing PRO data, should be reported to help readers interpret the PRO results and assess potential for bias.

PRO Elaboration – Results Item 15

CONSORT 2010:

Table showing baseline demographic and clinical characteristics for each group.

PRO Extension 2013:

Including baseline PRO data when collected.

Explanation:

Baseline PROs data may be used by clinicians and policy makers to assess the relevance and generalizability of trial findings.

PRO Elaboration – Results Item 17a

CONSORT 2010:

For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval).

PRO Extension 2013:

For multidimensional PROs, results from each domain and time point specified for analysis.

Explanation:

The potential for selective reporting of PROs is increased because study measures often contain multiple scales and items. In general, all PRO results should be presented alongside other outcome data to facilitate the clinical integration of the important findings with other prespecified outcomes.

PRO Elaboration – Discussion Item 22

CONSORT 2010:

Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence.

PRO Extension 2013:

PRO data should be interpreted in relation to clinical outcomes including survival data, where relevant.

Explanation:

The clinical significance of PRO results is often not discussed in RCT reports but should be interpreted in relation to other important clinical outcomes such as survival, especially in trials for which there are clinically relevant trade-offs between PROs and survival outcomes.

Implications of Using CONSORT-PRO Guidance

- Improved PRO reporting in clinical trials will enable robust evidence to inform patient choice, aid clinical decision making, and inform health policy

- Active implementation by journals, authors, and reviewers may lead to improved reporting

- PRO reporting is intrinsically linked to study design. Consider design in relation to:
  - FDA Guidance on PROs - https://www.fda.gov/media/77832/download
  - Spirit Initiative - https://www.spirit-statement.org/

Recap

- The final CONSORT PRO guidance identifies 5 items to be reported in all RCTs in which PROs are a primary or important secondary outcome

- An extension was deemed unnecessary for a number of existing CONSORT checklist items, however an elaboration of items that apply to PROs are recommended

- It is recommended that the CONSORT PRO guidance supplement the standard CONSORT guidelines for reporting RCTs with PROs as primary or secondary outcomes

Further Reading

Brundage M, Bass B, Davidson J et al. Patterns of reporting health-related quality of life outcomes in randomized clinical trials: implications for clinicians and quality of life researchers. *Qual Life Res.* 2011; 20(5): 653-664.

Brundage M, Blazeby J, Revicki D et al. Patient Reported Outcomes in Randomized Clinical Trials: Development of ISOQOL Reporting Standards. *Qual Life Res* 2012; 22(6): 1161-75.

Moher D, Hopewell S, Schulz KF et al. CONSORT 2010 explanation and elaboration: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340:c869.

Schulz KF, Altman DG, Moher D, CONSORT Group. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. *BMJ* 2010; 340:c332.

Calvert M, Blazeby J, Altman DG, et al, for the CONSORT PRO Group. Reporting of Patient-Reported Outcomes in Randomized Trials: The CONSORT PRO Extension. *JAMA* 2013; 309(8): 814-22.

Calvert M, Kyte D, Mercieca-Bebber R, et al, for the SPIRIT-PRO Group. Guidelines for inclusion of Patient-Reported Outcomes in Clinical Trial Protocols The SPIRIT-PRO Extension. *JAMA* 2018;319(5):483-494.


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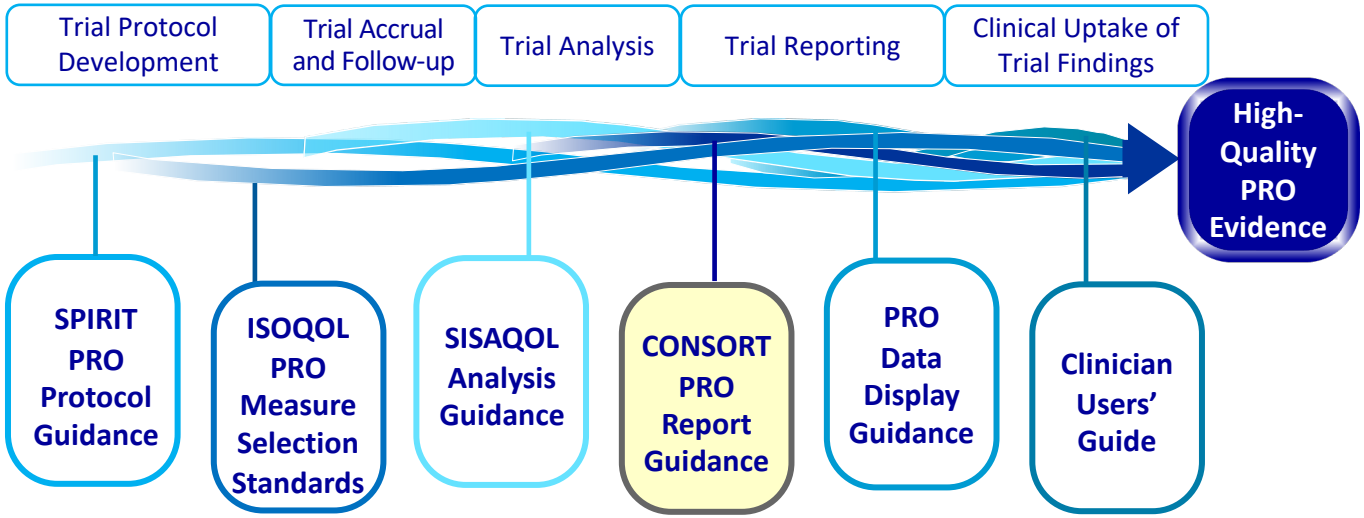

Overview of Tool Recommendations

How to Apply the Tools