


Establishing international standards in the analysis of patient reported outcomes and health-related quality of life data in cancer clinical trials

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What is the purpose of patient-reported outcome data (PRO)?

- 1 Collected directly from the patient- may be the only way of assessing and demonstrating treatment benefits (e.g. pain therapy, fatigue, sleep disturbances)
- 2 PRO/QoL data are the most relevant outcome data to patients in addition to overall survival
- 3 Offer additional information about the benefit/risk profile of a drug
- 4 May support the use of surrogate endpoints
- 5 By achieving a PRO label claim, information about treatment benefit from a patient perspective can be incorporated in label text and hence will facilitate shared decision making
- 6 Support reimbursement and coverage decisions and by demonstrating patient relevance of treatment benefit and enables calculation of quality-adjusted life years (QALYs)
- 7 May also be used to monitor quality of medical care delivered to the patients in clinical practice



PRO Data are key for patient centric drug development and need to meet the methodological requirements of Regulatory and HTA authorities

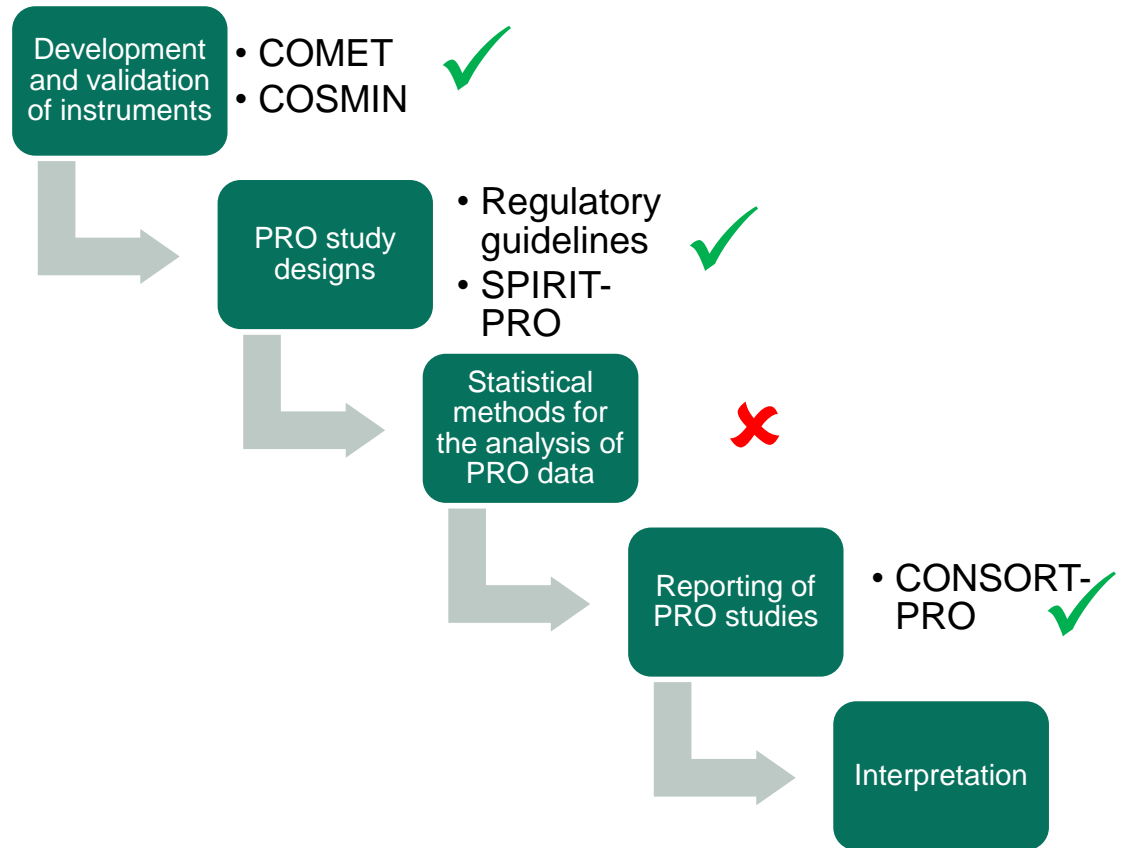
Why require HRQoL and PRO data special attention?

- Current regulatory guidelines suggest that the analytic considerations for HRQOL endpoints are similar to those for other trial endpoints (e.g., overall survival and progression free-survival)
- However these guidelines cannot easily be transposed to HRQOL studies.
- Data generated from HRQOL measures are much more complex: they
 - a) are multidimensional, with several subscales to characterize patients' symptoms and their impact on aspects of patient functioning
 - b) require repeated measurements in order to capture changes in HRQOL
 - c) are prone to missing data since it is often difficult to obtain complete HRQOL follow-up data from all randomized patients.

Current state of PRO and HRQoL in Oncology

Analyses often:

- lack clear HRQOL and other PRO research objectives
- lack standardization of basic statistical terms such as compliance and completion rates
- include a variety of statistical methods not always well justified with respect to analyzing HRQOL and other PRO data
- include a variety of approaches used to handle missing data
- may be using suboptimal statistical practices



Objectives of the full project



- **Achieve international consensus**, across stakeholders, on the optimal use of HRQOL and PRO data in cancer clinical trials;
- **Improve the quality of statistical analysis** of HRQOL and PRO data in cancer clinical trials;
- **Improve the standards of reporting of HRQOL and PRO data**, improve reliable interpretation, and ultimately faster dissemination, of HRQOL and PRO findings;
- **Ultimately, better use of these data** in regulatory approvals, HTA assessment, and shared decision-making.

Need for public-private collaboration



- This initiative aims to establish a multi-stakeholder consortium with the overall objective to standardise and develop recommendations for the analysis and interpretation of HRQOL and PRO data in cancer clinical trials.



- The focus of this topic is to achieve a consensus on the analysis methods of HRQOL and PRO data in RCTs and other novel trial designs.



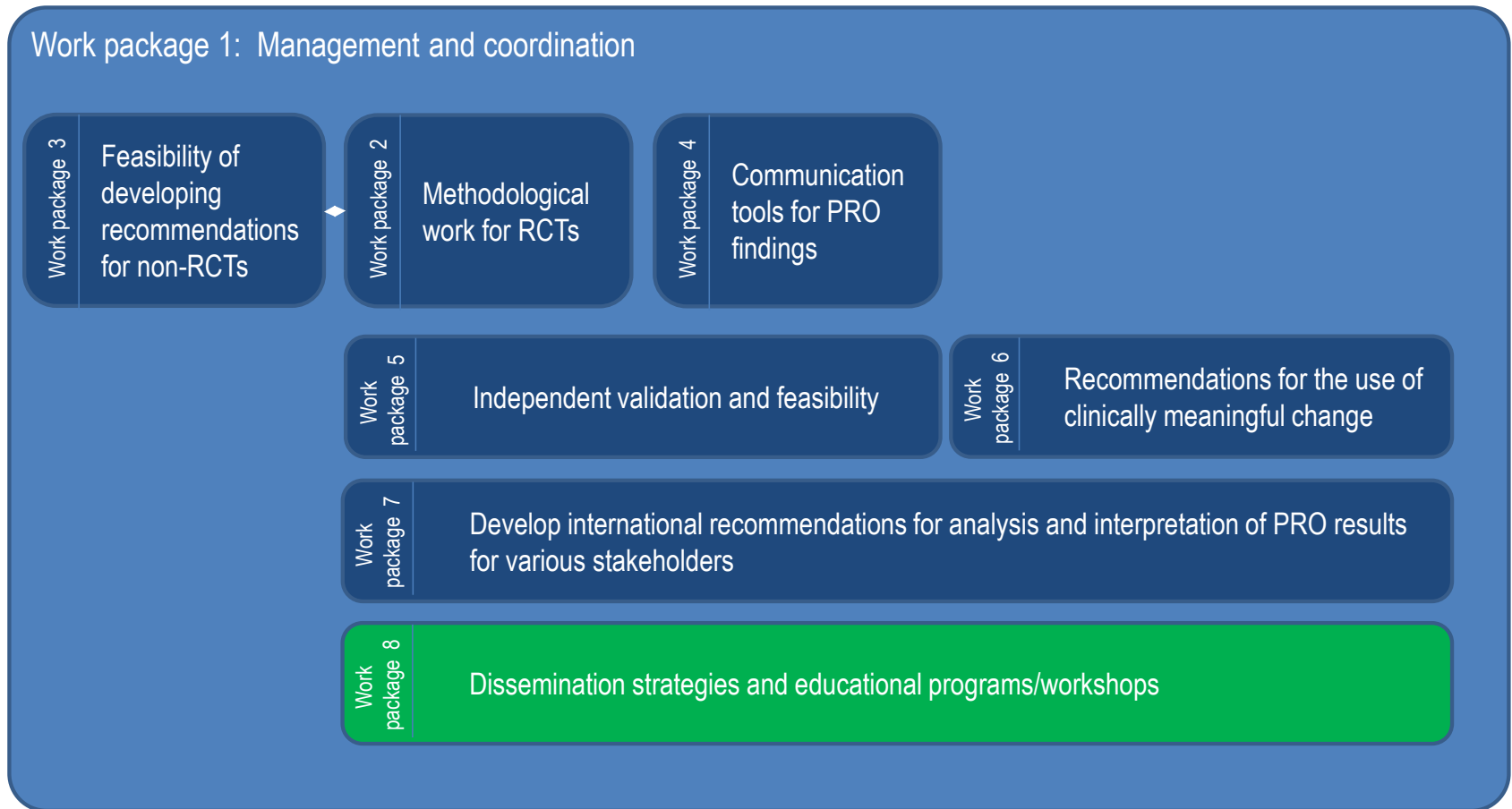
- To be able to address this challenge, the concerted efforts of different experts from various organisations are needed. It is critical to have a broad based consortium to include a wide range of experts and organisations:
 - patient groups and their representatives,
 - healthcare decision makers,
 - regulators and representatives from HTA authorities and other public health bodies are needed,
 - experts from the pharmaceutical industry.
 - clinicians
 - academics and PRO/QoL experts

Expected Impact

Reaching a broad international consensus is a prerequisite for a broader adoption of HRQOL and PRO data and is likely to result in:

- more reliable findings and faster dissemination of HRQOL and PRO data in cancer studies;
- advances in statistical science and improved statistical practice in cancer studies;
- improved interpretability of the data because of greater familiarity with standardised reporting;
- broader use and adoption of PRO data to inform benefit-risk evaluation in regulatory appraisals, added benefit evaluation in HTAs and reimbursement decision processes as well as shared treatment decision making contexts;
- better and improved shared decision making between patients and their treating physicians which may lead to improved patient satisfaction, an increased likelihood of adherence to treatment, higher likelihood of treatment success and a reduction in health-care cost;
- better and more efficient use of increasingly finite research and healthcare funding;
- improved and more efficient clinical trial designs that also investigate the cancer patient perspective on treatment outcomes.

Suggested architecture of the project



Expected contributions of the applicants

The applicant consortium will need to effectively combine the expertise of the various stakeholders in order to harmonise and standardise HRQOL and PRO analysis for cancer RCTs.

- The consortium should have representatives from these key stakeholders or demonstrate plans to bring in necessary stakeholders and in-depth knowledge, as appropriate:
 - regulatory affairs expertise with a proven track record of interacting with key regulatory agencies;
 - representatives from HTA agencies;
 - biostatisticians, epidemiologists, psychologists, and HRQOL and PRO researchers with experience in cancer RCTs (mandatory as participants);
 - clinicians and other health-care professionals with experience in the design and conduct of cancer randomised clinical trials;
 - representatives from academic medical and methodological societies;
 - experts in the visualisation and presentation of HRQOL and PRO data;
 - cancer patient advocacy groups, with knowledge and experience in cancer clinical

Expected contributions of the industry consortium

- In-depth knowledge of the advantages and disadvantages of various statistical methods and how they can be matched to identified research objectives;
- contributing to the review of clinically important responders and clinically important differences for various instruments and developing best practice recommendations for future instruments including outcome item banks;
- participation at all consensus meetings; making proposals, discussing options and contributing to guideline drafting and review;
- validating guideline recommendations by re-analysing existing data-sets and implementing them in prospective case studies;
- discussing and assessing the operational feasibility of implementing guideline recommendations in future cancer studies;
- contributing to developing educational tools and dissemination materials.

What's in it For You?

Academic researchers will have the ability to work collaboratively with industry to develop consensus recommendation that will eventually lead to a higher utilization of PRO data in decision making



SMEs as vendors will have access to state of the art PRO data and can contribute to develop novel communication tools



Patient organizations and associated Partners will be able share insights on their experiences with tumor-and treatment-related symptoms and QoL aspects and will be able to co-develop dissemination and education tools



Regulators, representatives from HTA organizations as well as payers will co-develop the consensus recommendation and will make sure that their requirements are reflected



Patients will ultimately benefit from better understanding of endpoints highly relevant to them and will be better equipped for shared decision making



Key deliverables of the full project

Work towards the development of internationally agreed consensus-based guidelines and recommendations for HRQOL and PRO analysis for RCTs, supported by relevant publications:

- a) recommendations to support the development of industry guidelines for the design, analysis and interpretation of HRQOL and PRO findings from cancer clinical trials;
- b) recommendations to support the development of regulatory guidance, such as European Medicines Agency (EMA) Points to Consider, and HTA guidelines for the design, analysis and interpretation of HRQOL and PRO findings from cancer clinical trials;
- c) recommendations to support the European Society for Medical Oncology (ESMO) and American Society of Clinical Oncology (ASCO) guidelines on assessing clinical benefit using HRQOL and PRO data from cancer trials;
- d) recommendations for dissemination strategies and educational programmes designed specifically to improve patients' understanding of HRQOL/PRO and empower their abilities for shared decision making;
- e) recommendations for clinically meaningful change for HRQOL/PRO instruments used in cancer clinical trials.