Publication planning and patient-reported outcomes: Demonstrating value in a multi-stakeholder era

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Abstract
Patient-reported outcomes (PROs) are an essential element to demonstrate the value of a health intervention. In many ways, PROs represent the ultimate “real-world” data, yet the drive towards “Big Data” has focused on routinely collected data from healthcare databases, which often do not include assessments of PROs or the patient voice. Effective planning of PRO publications requires an in-depth understanding of the planned studies, the opportunities these provide for publications, and how clinicians, patients, and caregivers may contribute as authors to provide validation of results. Mainstream clinical journals and conferences should be targeted wherever possible, considering the availability and objectives of “enhanced publication” options and open access to increase reach, comprehension, and impact. PRO publications must be written in a clear and engaging way, explaining the instrument in simple terms, and addressing the “so what?” question – ideally with an accompanying plain language summary. And PRO publications must always thank the patients.
The basic principles of publication planning are simple: to deliver the right data to the right audience at the right time. From a pharmaceutical company perspective, publication planning has traditionally focused on the clinical study programme; because pharma companies are required to register the clinical studies they conduct and to disseminate the results in a timely fashion, effective publication planning aims to publish data as soon as needed, with the greatest possible impact. Key considerations have therefore been “who” (authorship), “when” (timing), and “where” (journal/conference selection).

But while these principles still apply, publication planning has evolved to address ongoing changes in the landscape of healthcare decision makers, and their different demands for data. This article summarises why publications on patient-reported outcomes (PROs) are an essential element to demonstrate the value of a health intervention, and how PRO publications can be planned optimally, giving guidance on best practices for communicating PRO data effectively.

Why publications on PROs are essential to demonstrating value

Pharma publications teams previously focused on the clinical development programme, with publications of “other” studies – for example health economics, epidemiology, outcomes research, real-world evidence (RWE), and PROs – typically being left to the respective individual functions to develop. However, healthcare decision-making now involves a range of stakeholders – including physicians, payers, patients, and policy makers – each of whom has different definitions of value. Publication planning must therefore go beyond the clinical benefits of a health intervention, utilising all the available evidence to demonstrate fully its value from an economic, social, behavioural, and policy perspective.

PROs can provide direct insights into clinical outcomes in many conditions, but also offer particular insights into the impact of a disease and potential treatments on patients and caregivers from a social perspective (e.g. humanistic outcomes, such as quality of life and daily functioning), and from a behavioural perspective (e.g. individual and emotional drivers, such as perception of benefit/risk, treatment experience, and adherence).

In many ways, PROs represent the ultimate in “real-world” outcomes – and yet the drive towards RWE and “Big Data” has increased the application of routinely collected data from healthcare databases, which often do not include assessments of PROs or the patient voice at all. In addition, patients and caregivers are increasingly accessing specialist literature directly – which brings opportunities to reach these key audiences, but also challenges in ensuring comprehension. It is therefore as important now as it has ever been to include PRO studies in publication planning.

Understanding the range of publication opportunities for PROs

PRO studies offer much more scope for publication than simply reporting the PRO endpoints of a clinical trial in the primary article. Development of a new PRO instrument – or validation and application of an existing PRO instrument in a new indication or patient population – offers a wide range of publication opportunities that are not always recognised in publication planning (Table 1).

Publication planning must go beyond the clinical benefits of a health intervention to demonstrate its value from an economic, social, behavioural, and policy perspective.

<table>
<thead>
<tr>
<th>Identified need</th>
<th>Publication opportunity</th>
<th>Example publication</th>
</tr>
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<tbody>
<tr>
<td>Find out what PRO instruments are already available</td>
<td>Systematic literature review</td>
<td>Vakil et al.4</td>
</tr>
<tr>
<td>Develop conceptual framework and draft PRO instrument</td>
<td>Patient and physician focus groups and cognitive interviews</td>
<td>Jones et al.5</td>
</tr>
<tr>
<td>Confirm conceptual framework and assess properties of PRO instrument</td>
<td>Validation study in relevant patient samples</td>
<td>Jones et al.6</td>
</tr>
<tr>
<td>Collect, analyse, and interpret PRO data from patients</td>
<td>Clinical trials incorporating PRO endpoints</td>
<td>Mitchell et al.7</td>
</tr>
<tr>
<td>Utilise PRO data to determine patient health state utilities</td>
<td>Mapping study of PRO instrument to generic HRQoL/utility measure</td>
<td>Kay et al.8</td>
</tr>
<tr>
<td>Modify PRO measure for wider usage</td>
<td>Cultural adaptations, translations, evaluations in related diseases</td>
<td>Hongo et al.9</td>
</tr>
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</table>

Abbreviations: HRQoL, health-related quality of life; PRO, patient-reported outcome.
Publication planning and patient-reported outcomes – White

Guidance on publication planning for PROs

1. Identifying which PRO data can be published

A key first step in publication planning for PROs is to assess what studies will be performed, and to consider the publication opportunities that these provide. Table 1 provides a brief overview of different types of publication that can be developed from PRO studies, and here it is essential to take into account the perspective of the target audiences. For example, if the PRO instrument(s) being used have been newly developed, or are being used for the first time in a new indication, then the publication plan will need to include articles that introduce the PROs to the audience and provide the context that explains why they were developed and how they work. Conversely, if the PRO instrument is already well established in the disease area, then it may be more appropriate to plan articles that review previous publications of PRO data in that indication, to provide context for the new studies that are to come.

The process for identifying potential PRO publications starts with close review of clinical trial protocols (which should ideally have PRO endpoints described in line with SPIRIT-PRO guidelines)\(^ {21}\) to identify which PRO data will ultimately come from RCTs – because the publication plan should aim to “set the scene” and provide appropriate context for these results. The next step is to review plans for specific patient outcome studies led by other internal functions; these vary from company to company, but typically include a specialist PRO or Patient Centricity/Engagement function, or come under the wider remit of Health Economics and Outcomes Research (HEOR). Taking a collaborative, cross-functional approach to publication planning is particularly important for PRO data, in order to coordinate efforts and avoid communications being developed in inconsistent and siloed fashion.

2. Engaging with the right authors

A publication on PRO data from a multi-centre clinical trial will typically be authored by members of the writing committee for that study, alongside relevant representatives from the sponsor company (e.g. the responsible Medical Director and Study Statistician), following the International Council of Medical Journal Editors (ICMJE) guidelines on authorship.\(^ {22}\) ICMJE guidelines also cover other types of PRO publication (such as systematic literature reviews on the use of PROs, patient-level qualitative research, validation studies), but authorship of these may be less easy to determine. PRO studies are commonly outsourced to specialist vendors, and so it is common – but not best practice – for authorship of PRO publications to be limited to relevant representatives from the vendor and the sponsor company (e.g. the HEOR or PRO lead).

Best practice tips – authorship

Help communicate the clinical relevance of the PRO data through:

- involvement of clinicians as authors, to give essential clinical perspective and validation of the practical relevance of PRO data
- involvement of patients/caregivers as authors, where appropriate, to provide validation that the PRO data are reflective of their individual “real life” experience

Inclusion of clinicians and patients/caregivers as authors can be particularly effective for interview- or survey-based research.\(^ {23,24}\) Planning for clinician/patient/caregiver input at an early stage ensures that the authors can contribute fully to the study and publication, and thus meet ICMJE criteria for authorship.

3. Targeting the right journals and conferences

Fundamentally, the “right” journal or conference for any publication is the option that gives maximum exposure of the data to the most appropriate target audience in the timeliest fashion. Although there are a number of technical journals and conferences focused on PROs, growing interest in the patient voice among physicians, patients, payers, and other decision makers means that such journals and conferences should not necessarily be the default choice for PRO publications, because they typically do not reach these audiences.

Best practice tips – journal selection

Target PRO data directly to physicians, patients, payers, and other decision makers by:

- submitting PRO data to mainstream clinical journals and conferences, wherever possible, and reserving technical journals and conferences for methodologic aspects
- publishing full papers open access, enabling interested parties to obtain the relevant full articles without having to pay for them

The process for selecting target journals for PRO data needs to go beyond the usual parameters that are assessed in clinical study publication planning (e.g. impact factor, lead times, and geography). Careful research is required into aspects such as a journal’s receptiveness to PRO publications, their prior record of publishing different types of PRO study, and whether the editorial board includes academic expertise in PROs, to ensure meaningful peer review.

4. Writing up PRO studies in a clear and engaging way

Although writing the PRO publications per se is strictly outside the scope of publication planning, some guidance here is pertinent because even the best-laid plans will fail – that is, the journal articles or conference abstracts will be rejected – if the PRO data are not presented in a clear and engaging way. It is essential to consult reporting standards for PRO data, such as CONSORT-PRO or those developed by the International Society for Quality of Life Research (ISOQOL),\(^ {25,26}\) and guidance from learned societies such as the International Society for Pharmaeconomics and Outcomes Research.\(^ {27}\)

Following guidance from regulatory bodies (FDA and EMA) on the validation of PRO instruments is also advisable, and is particularly important if the PRO data are intended to support a label
5. Going beyond the publication

As with all highly technical disciplines, publications on PRO data benefit greatly from supplementary information – or “enhanced publication options” – that can help non-specialists understand the results. Going beyond the conference presentation or journal article is therefore essential for PRO data.

**Best practice tips – enhanced publication options**

Select publication enhancements according to the objectives that they can achieve:

- **enhance comprehension**, support with education-focused additional materials and formats (e.g. plain language summary, explanatory videos)
- **increase reach**, engage available channels (e.g. media, email, healthcare practitioner (HCP) community communications, and social sharing as appropriate)
- **drive real-world clinical impact**, translate the evidence into action with tools (e.g. apps, decision algorithms).

For PRO publications, the primary concern is generally to enhance comprehension; PROs are poorly understood and their application to clinical practice is often unclear. Increasing reach is important if the initial publication is unlikely to be read by all intended audiences (e.g. an article in a technical PRO journal will not be read by clinicians). Driving impact may be a consideration where there is potential for enhancing clinical adoption of a PRO instrument.

The most obvious supplementary element for a PRO publication is the plain language summary (PLS – an acronym that is also used for “patient lay summary”). Although EMA guidelines require a PLS to be posted for all clinical studies30, and this may include PRO data – the EMA PLS template is not particularly suited to explaining the technical and methodologic aspects of PRO studies. Given that regulatory guidelines do not mandate a PLS for other types of PRO study, it is recommended that a PRO publication is accompanied by a specifically tailored PLS that describes the study in a clear and engaging manner, covering the issues noted in the previous section. For journal articles, a PLS can often be provided as a peer-reviewed supplementary document associated with the article.

Other explanatory materials to accompany a publication could include an infographic summary, author video, animation, interactive annotated publication, and glossary of terminology, to name just a few examples. In addition to helping explain the study and aid understanding of its outcomes, these can provide a powerful stimulus to social sharing, and thereby help communicate to audiences who may not access the original publication. For journal articles, these should ideally be peer-reviewed supplementary materials associated with the article. For conference presentations, a number of options (including augmented reality, which provides a link from physical materials to embedded digital content) can enable access to these supplementary materials.

To maximise effectiveness, choice of the type of material should not only be guided by the tactical objectives (comprehension, reach, or impact) but also closely integrated with wider medical affairs communication planning. In all cases, compliance with relevant regulatory and promotional guidelines on the dissemination of data is of course essential, but is rarely prohibitive. With respect to the patient perspective, a good example of enhanced publication elements (summary slides and author video)31 accompanies an article reporting qualitative research on patient and physician perspectives in multiple sclerosis23,24.

**Never, ever forget …**

... that any publication of any study involving patients, should thank patients for their contribution. A short statement in the Acknowledgements section of a conference presentation or journal article is simple to do, but will be hugely valued.

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The author is employed by, and is a shareholder of, Oxford PharmaGenesis, a HealthScience communications consultancy that provides services to pharmaceutical, medical device, nutraceutical, and diagnostic companies.

References


