

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



## Richard White

Oxford PharmaGenesis, Oxford, UK;  
Green Templeton College, University of Oxford,  
Oxford, UK

## Correspondence to:

Richard White  
Oxford PharmaGenesis  
Tubney Warren Barn  
Tubney, Oxford  
OX13 5QJ, UK  
Tel. +44 1865 390144  
richard.white@pharmagenesis.com

## 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,<sup>1,2</sup> 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.<sup>3</sup>

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).

It is common practice early in the development process, when planning for the inclusion of PROs in a clinical study programme, to conduct a systematic literature review of the use of PRO instruments in the indication/patient population of interest. Such reviews have traditionally been considered internal fact-finding and have not been published, but actually provide essential “due diligence” to support

the choice of PRO instrument for subsequent studies.<sup>4,10,11</sup> Similarly, there is increasing demand for PRO results from randomised controlled trials (RCTs) or RWE studies as standalone publications, even when the top line data have been disclosed in a primary

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 1. Development and utilisation of PRO instruments provides a wide range of publication opportunities**

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

Abbreviations: HRQoL, health-related quality of life; PRO, patient-reported outcome.

publication.<sup>12–14</sup> Qualitative data (such as thematic interviews), preference studies, and surveys of patients and caregivers are also often overlooked as a potential source of publications – yet such studies provide important context to the impact of a disease and its treatment on patients and caregivers, and are also increasingly in demand from mainstream peer-reviewed journals.<sup>15–20</sup>

## 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)<sup>21</sup> to identify what 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.<sup>22</sup> 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.<sup>23,24</sup> 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),<sup>25,26</sup> and guidance from learned societies such as the International Society for Pharmacoeconomics and Outcomes Research.<sup>27</sup> 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

claim. Where appropriate, qualitative studies on patient experience and outcomes should be written in line with relevant general standards such as SRQR (Standard for Reporting Qualitative Research) and using specific standards for individual methodologies, for example COREQ (COnsolidated criteria for REporting Qualitative research) for interviews and focus groups.<sup>28,29</sup> Beyond these frameworks, there are several simple steps that can be taken to make PRO data easier to understand for a non-specialist.

### Best practice tips – writing PRO publications in a clear and engaging way

- **Explain technical terms or jargon when they are first introduced.**
  - Ideally one simple sentence, with a glossary if appropriate.
- **Outline briefly how the PRO instrument works.**
  - How and when is it administered, and to whom? What domains are included? How are they scored? What is normal vs mild/moderate/severe disease? Is improvement an increase or decrease in the score?
- **Address the “so what” question.**
  - How do changes in PRO scores relate to meaningful functional improvements? Do threshold/subgroup analyses express the data more usefully than group means? What is the clinically important difference?
- **Apply measures of readability to the publication.**
  - The Flesch or Flesch-Kincaid scoring system can be helpful, as can metrics such as the average number of words per sentence and the average number of syllables per word.

### 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, health-care 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 studies<sup>30</sup> – 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)<sup>31</sup> accompanies an article reporting qualitative research on patient and physician perspectives in multiple sclerosis.<sup>23,24</sup>

### 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.

### Acknowledgements

The author would like to thank Drs Polly Field, Tomas Rees, Martin Callaghan, and Chris Winchester (all of Oxford PharmaGenesis) for helpful discussions and critical review of the draft manuscript. This article summarises material previously disseminated by the author in podium presentations and workshops at annual meetings of the International Society for Medical Publications

Professionals and The International Publication Planning Association.

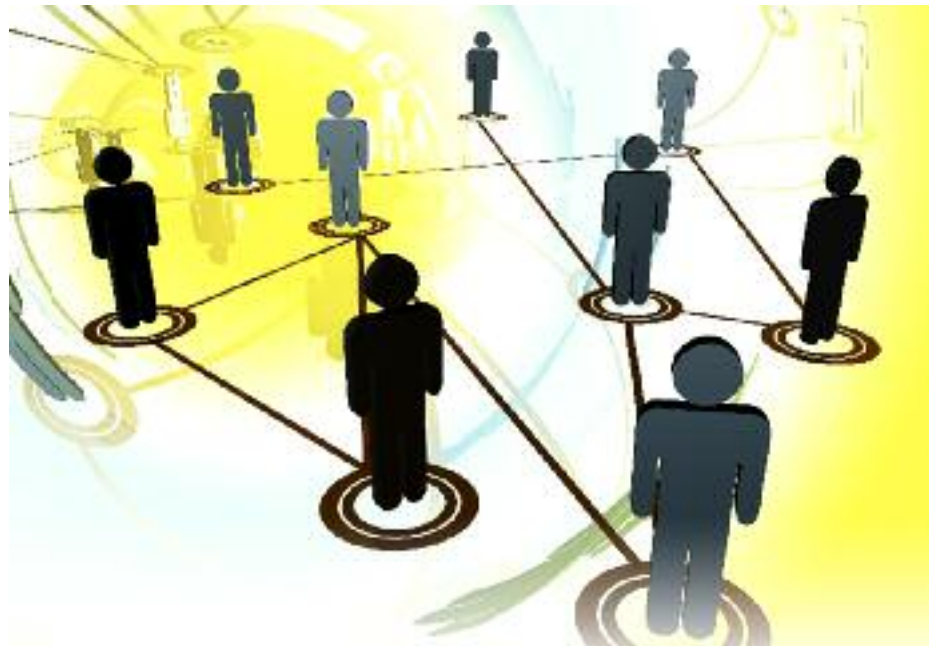
Going beyond the conference presentation or journal article is essential for PRO data.

## Conflicts of interest

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

1. United States Government. Clinical trials registration and results information submission. Final rule [Internet]. 2016 [cited 2018 Sep 6]. Available from: <https://www.federalregister.gov/documents/2016/09/21/2016-22129/clinical-trials-registration-and-results-information-submission>.
2. European Commission. Commission Guideline – Guidance on posting and publication of result-related information on clinical trials in relation to the implementation of Article 57(2) of Regulation (EC) No 726/2004 and Article 41(2) of Regulation (EC) No 1901/2006. 2012 [cited 2018 Sep 6]. Available from: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2012\\_302-03/2012\\_302-03\\_en.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2012_302-03/2012_302-03_en.pdf).
3. White R, Willett J, Field P. HEOR: why it is changing the world of medical publications. The MAP newsletter [Internet]. 2017 [cited 2018 Sep 6]. Available from: <https://ismpp-newsletter.com/2017/03/14/heor-why-it-is-changing-the-world-of-medical-publications/>.
4. Vakil NB, Halling K, Becher A, Ryden A. Systematic review of patient-reported outcome instruments for gastroesophageal reflux disease symptoms. *Eur J Gastroenterol Hepatol*. 2013;25(1):2–14. 10.1097/MEG.0b013e328358bf74.
5. Jones R, Junghard O, Dent J, Vakil N, Halling K, Wernersson B, et al. Development of the GerdQ, a tool for the diagnosis and management of gastroesophageal reflux disease in primary care. *Aliment Pharmacol Ther*. 2009;30(10):1030–8. 10.1111/j.1365-2036.2009.04142.x.
6. Jones R, Coyne K, Wiklund I. The gastroesophageal reflux disease impact scale: a patient management tool for primary care. *Aliment Pharmacol Ther*. 2007;25(12):1451–9. 10.1111/j.1365-2036.2007.03343.x.
7. Mitchell P, Bressler N, Tolley K, Gallagher M, Petrillo J, Ferreira A, et al. Patient-reported visual function outcomes improve after ranibizumab treatment in patients with vision impairment due to diabetic macular edema: randomized clinical trial. *JAMA Ophthalmol*. 2013;131(10):1339–47. 10.1001/jamaophthalmol.2013.4592.
8. Kay S, Ferreira A. Mapping the 25-item National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) to EQ-5D utility scores. *Ophthalmic Epidemiol*. 2014;21(2):66–78. 10.3109/09286586.2014.888456.
9. Hongo M, Kinoshita Y, Shimozuma K, Kumagai Y, Sawada M, Nii M. Psychometric validation of the Japanese translation of the Quality of Life in Reflux and Dyspepsia questionnaire in patients with heartburn. *J Gastroenterol*. 2007;42(10):807–15. 10.1007/s00535-007-2098-9.
10. Talley NJ, Wiklund I. Patient reported outcomes in gastroesophageal reflux disease: an overview of available measures. *Qual Life Res*. 2005;14(1):21–33.
11. Chassany O, Shaheen NJ, Karlsson M, Hughes N, Ryden A. Systematic review: symptom assessment using patient-reported outcomes in gastroesophageal reflux disease and dyspepsia. *Scand J Gastroenterol*. 2012;47(12):1412–21. 10.3109/00365521.2012.712999.
12. Nagy P, Hage A, Coghill DR, Caballero B, Adeyi B, Anderson CS, et al. Functional outcomes from a head-to-head, randomised, double-blind trial of lisdexamfetamine dimesylate and atomoxetine in children and adolescents with attention-deficit/hyperactivity disorder and an inadequate response to methylphenidate. *Eur Child Adolesc Psychiatry*. 2016;25(2):141–9. 10.1007/s00787-015-0718-0.
13. Calkwood J, Cree B, Crayton H, Kantor D, Steingo B, Barbato L, et al. Impact of a switch to fingolimod versus staying on glatiramer acetate or beta interferons on patient- and physician-reported outcomes in relapsing multiple sclerosis: post hoc analyses of the EPOC trial. *BMC Neurol*. 2014;14:220. 10.1186/s12883-014-0220-1.
14. Hunter SF, Agius M, Miller DM, Cutter G, Barbato L, McCague K, et al. Impact of a switch to fingolimod on depressive symptoms in patients with relapsing multiple sclerosis: An analysis from the EPOC (Evaluate Patient Outcomes) trial. *J Neurol Sci*. 2016;365:190–8. 10.1016/j.jns.2016.03.024.
15. Bakhai A, Sandberg A, Mittendorf T, Greiner W, Oberdiek AM, Berto P, et al. Patient perspective on the management of atrial fibrillation in five European countries. *BMC Cardiovasc Disord*. 2013;13:108. 10.1186/1471-2261-13-108.
16. Fridman M, Banaschewski T, Sikirica V, Quintero J, Erder MH, Chen KS. Caregiver perspective on pediatric attention-deficit/hyperactivity disorder: medication satisfaction and symptom control. *Neuropsychiatr Dis Treat*. 2017;13:443–55. 10.2147/NDT.S121639.





17. Muller-Lissner S, Tack J, Feng Y, Schenck F, Specht Gryp R. Levels of satisfaction with current chronic constipation treatment options in Europe – an internet survey. *Aliment Pharmacol Ther.* 2013;37(1):137–45. 10.1111/apt.12124.
18. Price D, Fletcher M, van der Molen T. Asthma control and management in 8,000 European patients: the REcognise Asthma and LInk to Symptoms and Experience (REALISE) survey. *NPJ Prim Care Respir Med.* 2014;24:14009. 10.1038/npjpcrm.2014.9.
19. Ryden A, Martin M, Halling K, Niklasson A. Night-time symptoms and their impact on sleep in patients with gastroesophageal reflux disease who have a partial response to proton pump inhibitors: a qualitative patient interview study. *Patient.* 2013;6(4):307–14. 10.1007/s40271-013-0024-1.
20. Price DB, Roman-Rodriguez M, McQueen RB, Bosnic-Anticevich S, Carter V, Gruffydd-Jones K, et al. Inhaler errors in the CRITIKAL study: type, frequency, and association with asthma outcomes. *J Allergy Clin Immunol Pract.* 2017;5(4):1071–81 e9. 10.1016/j.jaip.2017.01.004.
21. Calvert M, Kyte D, Mercieca-Bebber R, Slade A, Chan AW, King MT, et al. Guidelines for inclusion of patient-reported outcomes in clinical trial protocols: the SPIRIT-PRO extension. *JAMA.* 2018;319(5):483–94. 10.1001/jama.2017.21903.
22. International Committee of Medical Journal Editors. Recommendations for the conduct, reporting, editing, and publication of scholarly work in medical journals. [cited 2018 Sep 6]. Available from: <http://www.icmje.org/icmje-recommendations.pdf>.
23. Kantor D, Bright JR, Burtchell J. Perspectives from the patient and the healthcare professional in multiple sclerosis: social media and participatory medicine. *Neurol Ther.* 2018;7(1):37–49. 10.1007/s40120-017-0088-2.
24. Kantor D, Bright JR, Burtchell J. Perspectives from the patient and the healthcare professional in multiple sclerosis: social media and patient education. *Neurol Ther.* 2018;7(1):23–36. 10.1007/s40120-017-0087-3.
25. Calvert M, Blazeby J, Altman DG, Revicki DA, Moher D, Brundage MD, et al. Reporting of patient-reported outcomes in randomized trials: the CONSORT PRO extension. *JAMA.* 2013;309(8):814–22. 10.1001/jama.2013.879.
26. Brundage M, Blazeby J, Revicki D, Bass B, de Vet H, Duffy H, et al. Patient-reported outcomes in randomized clinical trials: development of ISOQOL reporting standards. *Qual Life Res.* 2013;22(6):1161–75. 10.1007/s11136-012-0252-1.
27. International Society For Pharmacoeconomics and Outcomes Research. Good practices for outcomes research. 2018 [cited 2018 Sep 6]. Available from: <https://www.ispor.org/heor-resources/good-practices-for-outcomes-research>.
28. O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. Standards for reporting qualitative research: a synthesis of recommendations. *Acad Med.* 2014;89(9):1245–51. 10.1097/ACM.0000000000000388.
29. Tong A, Sainsbury P, Craig J. Consolidated criteria for reporting qualitative research (COREQ): a 32-item checklist for interviews and focus groups. *Int J Qual Health Care.* 2007;19(6):349–57. 10.1093/intqhc/mzm042.
30. European Medicines Agency. Summaries of clinical trial results for laypersons. 2018 [cited 2018 Sep 6]. Available from: [https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017\\_01\\_26\\_summaries\\_of\\_ct\\_results\\_for\\_laypersons.pdf](https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf).
31. Kantor D, Bright JR, Burtchell J. Perspectives from the patient and the healthcare professional in multiple sclerosis: social media and patient education. [Video interview]. 2018 [cited 2018 Sep 6]. Available from: [https://figshare.com/articles/Perspectives\\_from\\_the\\_Patient\\_and\\_the\\_Healthcare\\_Professional\\_in\\_Multiple\\_Sclerosis\\_Social\\_Media\\_and\\_Patient\\_Education/6210941](https://figshare.com/articles/Perspectives_from_the_Patient_and_the_Healthcare_Professional_in_Multiple_Sclerosis_Social_Media_and_Patient_Education/6210941).

### Author information

**Richard White** is Chief Operating Officer at Oxford PharmaGenesis and a member of Green Templeton College, University of Oxford. Richard speaks widely at international meetings on publications and communications related to the patient perspective, PROs, health economics and RWE, and was Chair of the 2017 and 2018 annual meetings of The International Publication Planning Association.