

The importance of patient-reported outcomes in cancer studies

Retzer, Ameeta; Kyte, Derek; Calman, Lynn; Glaser, Adam; Stephens, Richard; Calvert, Melanie

DOI:

[10.1080/23809000.2018.1472524](https://doi.org/10.1080/23809000.2018.1472524)

License:

None: All rights reserved

Document Version

Peer reviewed version

Citation for published version (Harvard):

Retzer, A, Kyte, D, Calman, L, Glaser, A, Stephens, R & Calvert, M 2018, 'The importance of patient-reported outcomes in cancer studies', *Expert Review of Quality of Life in Cancer Care*, vol. 3, no. 2-3, pp. 65-71. <https://doi.org/10.1080/23809000.2018.1472524>

[Link to publication on Research at Birmingham portal](#)

Publisher Rights Statement:

Checked for eligibility: 28/01/2019

This is an Accepted Manuscript of an article published by Taylor & Francis in Expert review of quality of life in cancer care on 09/05/2019, available online: <http://www.tandfonline.com/10.1080/23809000.2018.1472524>.

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

The importance of patient-reported outcomes in cancer studies

[Ameeta Retzer](#), [Derek Kyte](#), [Lynn Calman](#), [Adam Glaser](#), [Richard Stephens](#) & [Melanie Calvert](#)

Pages 65-71 | Received 01 Dec 2017, Accepted 26 Apr 2018, Accepted author version posted online: 02 May 2018, Published online: 09 May 2018

The importance of Patient-Reported Outcomes in cancer studies

1. Abstract

Introduction: Cancer incidence is increasing; one in two people in the UK are expected to develop cancer during their lifetime. However, survival rates of people living with cancer have improved over the last few decades. More than 50% of all UK cancer patients survive for beyond 10 years, this rate has doubled in the last 40 years.

Areas covered: This article provides a scientific review of the use of patient reported outcomes (PROs) to assess the short and longer term impact of cancer and treatment on patient quality of life and symptoms.

Expert opinion/commentary: There is increasing recognition that, in addition to survival and other clinical metrics, we need to understand more about the impact that cancer and its treatment has on the everyday lives of people living with and beyond cancer. Patients must have access to information around quality of life and survival with which they can make more informed decisions about their care. We need to understand more about the natural history of recovery and wellbeing and the contributory factors to identify those who are not doing well and to understand how we can support them better, plan appropriate services and support patients in making choices about treatment.

2. Introduction

The incidence of cancer is increasing; it is now expected that one in two people in the UK will develop cancer at some point in their lives¹. The survival rates of people living with cancer have improved over the last few decades. More than 50% of all cancer patients in the UK are surviving for beyond 10 years, this rate has doubled in the last 40 years². These improvements have been attributed to improved screening, earlier diagnosis and enhancements in, and access to, treatment. There are now 2.5 million people in the UK living with and beyond cancer³. The number of cancer survivors in the UK is projected to increase by approximately one million per decade (3% every year) resulting in four million people living with cancer in 2030³.

There is increasing recognition that, in addition to survival and other clinical metrics such as toxicity grading, we need to understand more about the impact that cancer and its treatment has on the everyday lives of people living with and beyond cancer. Patients must have access to information around quality of life and survival in tandem, with which they can make more informed decisions about their care⁴. People can experience a range of issues following a cancer diagnosis, during and

beyond treatment, such as problems with social relationships, poorer quality of life, psychological distress, disease recurrence and progression, physical symptoms and financial consequences⁵⁻⁸. The impact these issues can have on patients is variable; some people do well after cancer treatment and some experience short, medium and long term consequences. We need to understand more about the natural history of recovery and wellbeing and the contributory factors in order to identify those who are not doing well and to understand how we can support them better, plan appropriate services and support patients in making choices about treatment (or having no treatment). One way to assess the short and longer term impact of cancer and treatment on patient quality of life and symptoms is through the use of patient reported outcomes (PROs). PROs may be used in addition to traditional clinical data to supplement clinical findings and attain a holistic understanding of patients' status.

Patient reported outcome measures (PROMs) are standardised, validated questionnaires that are completed by patients to measure their perceptions of their own functional status and wellbeing. They can be used to measure patients' perceptions of their general health or in relation to specific diseases or conditions⁹. As such, PROMs can focus on physical symptoms, treatment toxicities, psychosocial problems or global health-related quality of life (HRQoL) and many other relevant constructs¹⁰. PRO capture ensures the patients' experience of cancer and treatment is represented in health measurement and when considering the effectiveness of clinical interventions^{11, 12}. Common non-cancer specific measures include the five dimension EuroQol questionnaire, the EQ-5D¹³ and the Hospital Anxiety and Depression Scale, the HADS¹⁴. Commonly used cancer-specific measures include the European Organisation for the Research and Treatment of Cancer Quality of Life Questionnaire¹⁵ and the Functional Assessment of Cancer Therapy scale¹⁶.

This article aims to provide a review of the use of PROs to assess the short and longer term impact of cancer and treatment on patient quality of life and symptoms. This is discussed first in the context of cancer research, then in routine cancer care, and lastly the next steps for PROs in cancer are considered.

3. PROs in Cancer Research

In cancer research, PROMs are used to measure the participants' assessment of the impact of a treatment or intervention upon their health condition, without interpretation of by a clinician or anyone else¹⁷. The complementary nature of PRO data when used in addition to other outcomes in trial settings has been demonstrated. It has been found that patients' reports better reflect daily health status and clinicians' assessments better predict unfavourable clinical events. When used in combination, both forms of data provide clinically pertinent information that warrants their inclusion in a trial¹⁸. PRO data collected in cancer studies can inform future patient choice and clinical decision-making, health technology assessment, health economic evaluations, labelling claims and healthcare policy and commissioning¹⁹⁻²¹; however this requires high quality PRO study design, rigorous data collection and appropriate reporting.

Patients are motivated to participate in clinical research due to the possibility of accessing a better form of treatment or that the trial results may benefit others²²⁻²³. Ethical practice in research dictates that data provided by participants is collected and reported to effectively contribute to the knowledge and practice in the field²⁴. However, research suggests that the collection of PROs from participants is often inconsistent, creating a potential source of bias in the resulting data²⁵. In

addition to this, a review of Health Technology Assessment trials funded by the National Institute for Health Research found that PRO-related information is commonly omitted from trial protocols, even where a PRO is the primary outcome, which may result in impaired data collection and poor quality data²⁶. This was reiterated by the most recent study of its kind, the EPiC study²⁷, which in its review of the cancer clinical trials on the UK National Institute for Health Research portfolio found that studies on average included less than one third of the recommended PRO-related items for study protocols²⁸, replicating findings from an earlier Australian study²⁹. In terms of reporting, a growing body of research suggests that PRO findings from cancer clinical trials are poorly reported by investigators in peer-review publications or not at all³⁰⁻³². The EPiC study findings indicate that more than one-third of trials fail to publish PRO data, despite having reported findings related to the primary outcome²⁸. Suggestions for future research regarding the collection, analysis and reporting of PRO data are explored in Box 1.

Box 1: Further questions for research, how is PRO data collected, analysed, and reported?

- Do terms such as, *quality of life* and *psychosocial outcomes*, need to be defined better in the research setting so that they can be measured and collected more effectively? In practice, these terms can be used interchangeably.
- How can we best identify outcomes of importance from the patients' perspective – so these can be incorporated in studies?
- How can PROs, such as QoL and psychosocial outcomes, be elevated in importance within a trial context when they are often chosen as secondary or exploratory objectives, following overall survival as primary? The quality of survival is overlooked.
- How can we facilitate the rapid analysis of PRO data so that the results can be interpreted alongside key clinical data such as survival?
- How can the wider infrastructure promote and support long-term collection and dissemination of PRO data? This might require a change of funding strategy by funding bodies.

Concerns about quality of data and poor reporting have clear implications for research findings reaching the necessary stakeholder groups, such as patients, clinicians, policy-makers and other researchers. Within these circumstances, the extent to which it may inform decision-making and changing practice is limited. Questions for future research relating to the use and dissemination of PRO data are presented in Box 2.

Reporting and disseminating research findings are undertaken for several reasons and via numerous channels³³. Publication of research via the peer-review process with the aim of informing academic audiences is one step in the dissemination process³⁴. However, for research findings to reach wider audiences and have greater impact³⁵, different strategies must be pre-planned and implemented³⁶⁻³⁸. Unfortunately, there are few established outlets for the publication of PRO data which are easily accessible by cancer patients and clinical groups.

Challenges encountered in the collection of PRO data may be addressed through the use of PRO specific guidelines to aid in the design and planning of cancer studies. Good research conduct and reporting may be upheld through the use of guidelines supporting high quality study protocols³⁶. In

addition to the SPIRIT (Standard Protocol Items: Recommendations for Interventional Trials) Statement, providing a list of items recommended for inclusion in trial protocols³⁹, the recently developed SPIRIT PRO Extension⁴⁰ details additional PRO-specific items recommended to facilitate the effective incorporation of PROs in trial design. However, for such guidelines to have an impact, widespread endorsement is necessary by, for example, funders, journals and regulators. In relation to reporting, regulatory bodies may also have a role in ensuring the complete publication of trial findings. An example of this is a yet to be adopted directive by the EU for results for all trial endpoints to be published within one year of trial completion⁴¹. International guidance for the transparent reporting of PRO data, the CONSORT-PRO extension⁴², may also be used by investigators and authors to aid in the quality and completeness of reports of PRO findings.

Box 2: Further questions for research, how is PRO data used and how could it be disseminated further?

- How can PRO data be incorporated more robustly in appraisals of new drugs or technologies – for licencing or in the UK NICE approval?
- How does PRO data affect clinical practice on a daily basis in terms of its implementation, impact and any subsequent improvements in care?
- How do patients currently access/use PRO data? Participants say, “Our data, our lives, how are we using it?”
- To what extent are patients currently involved in the dissemination process post-study? Is there a role for patients in championing findings and bringing PRO results to a broader audience?
- How might clinicians be encouraged to refer to PRO data to inform clinical practice and become consumers of this information? Are there currently under-used channels available or should new pathways be generated?

Beyond the immediate barriers to reporting, the changing global research setting may have as yet undetermined impacts upon the ongoing generation of PRO research, reporting and data use. An example of this is the case wherein the United Kingdom is poised to leave the European Union (EU), potentially posing barriers to continued data sharing⁴³ and collaboration in the field of cancer care and research⁴⁴. Secure cross-country data sharing underpins international research particularly for conditions such as rare diseases and paediatric cancers where small numbers require statistical power to be attained via use of an international sample⁴⁵.

The research landscape is also changing in such a way that may lead to a paradigm shift in terms of the focus of cancer studies. Significant progress in cancer survival in certain cancer types⁴⁶ may shift focus from overall or progression-free survival to quality of survival⁴⁷ in some areas. Data pertaining to the quality of survival for those living with and without cancer would underpin such work and the concept of “quality of survival” would need to be embedded in clinical trials and studies for this purpose.

4. PROs in Routine Cancer Care

PROs are being increasingly used as a component of routine practice. Their use in clinical settings has been associated with richer discussions of patient outcomes, improved symptom control, increased supportive care responses, patient satisfaction and wellbeing^{48,49}. While findings suggest that PRO data may predict prognosis in cancer clinical trials^{50,51}, research also indicates that their use in symptom monitoring during routine treatment is associated with increased survival compared with usual care⁵².

It is well established that cancer patients value information relating to treatments and their risks and benefits^{53,54}, and that such information aids patients in clarifying their treatment preferences⁵⁵⁻⁵⁷. For clinicians, PRO data may help facilitate patient-centred care^{58,59}, bridging patients' concerns with their own⁶⁰. As part of routine use in a clinical setting, PROMs can enhance the interaction between the healthcare provider and the individual, bringing about information due to the posing of questions that the clinician would not normally ask and topics that patients may not have chance to raise in a standard consultation. Using PROMs in routine practice can help increase the frequency with which issues related to health-related quality of life are discussed in consultations^{49,61}. These conversations can be sustained by the continued generation and reporting of PRO data in relation to treatments and interventions, providing answers to questions relating to how areas such as HRQoL might be addressed. PROs are increasingly being used as a means of patient surveillance and symptom monitoring during their receipt of care to promote overall survival and management of adverse events⁶²⁻⁶⁴.

5. Where Next for PROs in Cancer?

The potential use of PROs in clinical settings is becoming a topic of increasing interest. In England, the Independent Cancer Taskforce in their strategy for achieving better cancer outcomes have included the development of a quality of life metric to monitor and support people living with and beyond cancer⁶⁵. To this end, England will be the first country to routinely collect quality of life data from recovering cancer patients⁶⁶. This represents a new approach to improve care through the use of personalised plans informed by data relating to their needs in addition to the physical aspects of health, moving quality of life data to the heart of commissioning decisions. Within this model, psychosocial risk stratification could be used to direct individuals into specialised services that address needs.

Emphasis on patient-centred care is also reflected in national cancer policy and expectations of practice. In England, the National Cancer Patient Experience Survey focused on areas pertaining to patients' perception of their understanding and involvement in treatment decisions⁶⁷. Several questions reflected the expectation that patients should routinely be provided with information pertaining to side-effects and immediate and long term impacts of cancer and their respective treatment options⁶⁸. This is also echoed in the UK's National Cancer Strategy⁶⁹⁻⁷¹ published by an independent taskforce, clearly outlining the intention to address patients' reports of deficiencies in the information they were currently given regarding their treatment options in their five year plan. The American Society of Clinical Oncology has a PRO committee that is developing and testing PRO measures, which, in the future, may be used to assess quality within ASCO's Quality Oncology Practice Initiative⁷². These signal not only a shift in policy but the development of a structure of accountability that ensures changes in practice are maintained.

Despite indications of the continuing utility of PROs in cancer, particularly within some specific cancer sites⁷³⁻⁷⁶, there are some limitations pertaining to the measures themselves and their use in practice. These include their content validity⁷⁷ and sensitivity to domains relevant to patients and those living with and beyond cancer⁷⁸; and potential barriers to their delivery and implementation such as length and complexity of measures or burden on well and unwell patients⁷⁹.

6. Conclusion

PROs are commonly used in cancer research studies and are being increasingly used in routine practice. Health policy-makers are drawing upon PRO data and the generation of PRO data appears to be integrated more into routine practice than ever before, with resource allocation and clinical decision-making being informed by these data.

While the quality of the data collected in cancer clinical trials may limit their use in informing clinical care and health policy, the widespread adoption of guidelines by journals, funders, and research organisations may provide the solution by holding investigators to high standards of practice. To ensure research findings reach the necessary audiences, new avenues for dissemination must be identified so clinicians and patients are able harness PRO research and incorporate it into their decision-making and practice.

In the context of supporting those living with and beyond cancer, PRO data may be used in addition to other indicators, such as biomarkers and clinical tests, to signify the use of particular treatment strategies in the handling of survivorship-related disease. PRO data collected from these individuals also provides opportunity to use this information to indicate when further investigation is required through other clinical means.

7. Expert commentary

As has been identified throughout this paper, a key priority in the field of PROs is to uphold and promote best practice principles in the collection and reporting of PRO data so that the patients' perspective remains central to clinical trial outcomes and routine care. This is particularly important given the rapid evolution in the treatment of cancer and provision of care to those living with and beyond cancer.

Relevance and use of PROMs requires that they retain face, construct, and content validity, as well as reliability, and sensitivity to change in patients' conditions^{17, 80-83}, making their continuous revision an ongoing exercise. Ensuring their effective delivery and implementation with minimal burden upon participants is vital⁸⁴. Failure to do these would significantly undermine their utility in clinical trials and routine care settings, however the field has issued guidance to uphold good practice and promote effective use of PROMs⁸⁵⁻⁸⁷. The SPIRIT-PRO extension⁴⁰ aims to facilitate the collection of high-quality data that may inform patient-centred care by improving the PRO-related content in clinical trial protocols. These accompany the CONSORT-PRO extension⁴², recommended for use in addition to standard CONSORT guidelines⁸⁸ to enable robust interpretation of PRO findings from RCTs and inform patient care. However, the extent to which these may have an impact on practice is determined by their adoption and endorsement by key stakeholders.

Meanwhile, evidence continues to emerge emphasising the continued role of PROs in the early assessment of psychosocial factors following cancer. The CREW Cohort Study⁸⁹ demonstrated how

psychosocial factors prior to surgery predict recovery trajectories following cancer treatment independent of treatment or disease characteristics. These findings signify implications for the management of cancer and demonstrate how PROs may be used to identify support needs during the treatment phase, changing patient pathways, and improve recovery as a result.

8. Five-year view

Increasing levels of survival following cancer is resulting in greater numbers of cancer survivors, including those with incurable but treatable cancers, and greater diversity of experience among those individuals with specific and complex sets of needs. Managing and promoting the wellbeing of these groups requires an approach that incorporates consideration for their quality of life⁹⁰. For those involved in cancer research, this requires a shift in focus from commonly used outcomes such as overall survival, to outcomes that encompass the quality of survival. This is integral to the generation of an evidence base that may underpin future policy, practice, and treatment choices⁹¹. Data generating activities include initiatives including the global TrueNTH registry⁹² whereby care provided to men with localised prostate cancer may be monitored through the collection of PROs alongside clinical data. Five years from now, the cancer survival trend will necessitate continued research to better understand and support the changing needs of survivors.

9. Key issues

- Further research is needed on the impact that cancer and its treatment has on the everyday lives of people living with and beyond cancer.
- Patients must have access to information relating to quality of life and survival, with which they can make more informed decisions about their care. However, there are few established outlets for the publication of PRO data which are easily accessible by cancer patients and clinical groups.
- PROs may be used in addition to clinical data to supplement clinical findings and attain a holistic understanding of patients' status. However, research suggests that the collection of PROs from participants is often inconsistent, creating a potential source of bias in the resulting data.
- PROs are being increasingly used as a component of routine practice. Their use has been associated with richer discussions of patient outcomes, improved symptom control, increased supportive care responses, patient satisfaction and wellbeing.
- Continued efforts are required to ensure that PROMs remain sensitive to the needs of patients and barriers to their delivery and implementation are minimised.

10. References

1. Ahmad AS, Ormiston-Smith N, Sasieni PD (2015) Trends in the lifetime risk of developing cancer in Great Britain: comparison of risk for those born from 1930 to 1960. [Br J Cancer](#). 2015 Mar 3;112:943-7. doi: 10.1038/bjc.2014.606. Epub 2015 Feb 3

2. Cancer Research UK. Cancer Statistics for the UK. Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk#heading-Two> [Accessed 1.12.2017]
3. Maddams J, Utley M, Møller H. Projections of cancer prevalence in the United Kingdom, 2010-2040. *Br J Cancer* 2012; 107: 1195-202
4. Basch E. Toward Patient-Centered Drug Development in Oncology. *New England Journal of Medicine* 2013; July 3 DOI: 10.1056/NEJMp1114649
5. Corner J, Wright D, Hopkinson J, et al. The research priorities of patients attending UK cancer treatment centres: findings from a modified nominal group study. *Br J Cancer* 2007; 96: 875–81
6. Hewitt M, Rowland JH, Yancik R. Cancer survivors in the United States: age, health, and disability. *J Gerontol A Biol Sci Med Sci* 2003; 58: 82–91
7. Foster C, Haviland J, Winter J, et al. Pre-surgery depression and confidence to manage problems predict recovery trajectories of health and wellbeing in the first two years following colorectal cancer: results from the CREW cohort study. *PLoS One* 2016; 11: e0155434
8. Macmillan Cancer Support (2013). Throwing light on the consequences of cancer and its treatment. Available from: <https://www.macmillan.org.uk/documents/aboutus/research/researchandevaluationreport/s/throwinglightontheconsequencesofcanceranditstreatment.pdf> [Accessed 1.12.17]
9. Dawson J, Doll H, Fitzpatrick R, et al. The routine use of patient reported outcome measures in healthcare settings. *BMJ* 2010;340:c186
10. D. Howell, S. Molloy, K. Wilkinson, et al; Patient-reported outcomes in routine cancer clinical practice: a scoping review of use, impact on health outcomes, and implementation factors, *Annals of Oncology*, 2015; 26;1846-58
11. Klag MJ, MacKenzie EJ, Carswell CI, et al. Foreword: the role of the patient in promoting patient-centered outcomes research. *Patient* 2008; 1: 1–3
12. Osaba D. Translating the science of patient-reported outcomes assessment into clinical practice. *JNCI Monogr* 2007; 37: 5–11
13. Rabin R, Charro F. EQ-5D: a measure of health status from the EuroQol Group. *Ann Med.* 2001 Jul;33:337-43
14. Zigmond, A. S., & Snaith, R.P. (1983). The Hospital Anxiety And Depression Scale. *Acta Psychiatrica Scandinavica.* 1983; 67, 361-70
15. Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst.* 1993; 85:365-76
16. Cella DF, Tulsky DS, Gray G, et al. The Functional Assessment of Cancer Therapy scale: development and validation of the general measure. *J Clin Oncol.* 1993; 11:570-9
17. Food and Drug Administration (2009). Guidance for Industry – Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Available from: <https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf> [Accessed 1/12/17]
18. Basch E, Jia C, Heller G, et al. Adverse Symptom Event Reporting by Patients vs Clinicians: Relationships With Clinical Outcomes. *Journal of the National Cancer Institute* 2009; 101:1624-32
19. Higginson IJ, Carr AJ. Measuring quality of life: using quality of life measures in the clinical setting. *BMJ* 2001;322:1297–300
20. NICE. Guidance on the use of trastuzumab for the treatment of advanced breast cancer. National Institute for health and care excellence. Technology appraisal guidance [TA34] Available from: <https://www.nice.org.uk/guidance/ta34> [Accessed 6.10.17]
21. EMA. Reflection paper on the use of patient reported outcome (PRO) measures in oncology studies (Draft). European Medicines Agency 2014; Oncology Working Party; Doc. ref. EMA/CHMP/292464/2014

22. Moorcraft SY, Marriot C, Peckitt C, et al. Patients' willingness to participate in clinical trials and their views on aspects of cancer research: results of a prospective patient survey. *Trials* 2016; 17:17
23. Ellis PM, Attitudes towards and participation in randomised clinical trials in oncology: A review of the literature. *Annals of Oncology* 2000;11: 939-45
24. Chalmers I, Bracken MB, Djulbegovic B, et al. How to increase value and reduce waste when research priorities are set. *Lancet*. 2014;383:156–65
25. Kyte D, Ives J, Draper H, et al. Inconsistencies in Quality of life Data Collection in Clinical Trials: A Potential Source of Bias? Interviews with Research Nurses and Trialists. *PLOS One*. 2013;8:10
26. Kyte D, Duffy H, Fletcher B, et al. Systematic Evaluation of the Patient-Reported Outcome (PRO) Content of Clinical Trial Protocols. *PLoS ONE*. 2014;9:e110229
27. Ahmed K, Kyte D, Keeley T, et al. Systematic evaluation of patient-reported outcome (PRO) protocol content and reporting in UK cancer clinical trials: the EPiC study protocol. *BMJ Open* 2016;6:e012863. doi:10.1136/bmjopen-2016- 012863
28. Kyte D, Retzer A, Ahmed K, et al. 2017, Systematic Evaluation of Patient-Reported Outcome (PRO) Protocol Content and Reporting in Cancer Clinical Trials: The EPiC Study, Philadelphia USA, 18.10.2017. Available from: http://www.isoqol.org/UserFiles/AC17/AC17-FP_web.pdf [Accessed: 28.2.18]
29. Mercieca-Bebber R, Friedlander M, Kok PS, et al. The patient-reported outcome content of international ovarian cancer randomised controlled trial protocols. *Qual Life Res* 2016; 25: 2457-65
30. 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;20:653–64
31. Schandelmaier S, Conen K, von Elm E, et al. Planning and reporting of quality-of-life outcomes in cancer trials. *Ann Oncol* 2015;26:1966–73
32. Efficace F, Fayers P, Pusic A, et al. On behalf of EORTC Quality of Life Group. PROMOTION Registry. Quality of patient-reported outcome reporting across cancer randomized controlled trials according to the CONSORT PRO extension: a pooled analysis of 557 Trials. *Cancer* 2015;121:3335–42
33. Tabak RG, Siqueira Reis R, Wilson P, et al. Dissemination of health-related research among scientists in three countries: Access to resources and current practices. *BioMed Research International* 2015
34. McGowan J. Measuring most informative titles (declarative titles) as a knowledge translation dissemination tool is possible using altmetrics. *Journal of Clinical Epidemiology* 2017; 85: 12-13
35. Cruz Rivera S, Kyte DG, Aiyegbusi OL, et al. Assessing the impact of healthcare research: A systematic review of methodological frameworks. *PLoS Med* 2017; 14: e1002370. <https://doi.org/10.1371/journalpmed.1002370>
36. Peters DH, Adam T, Alonge O, et al. Implementation research what it is and how to do it. *BMJ* 2013; 347:f6753
37. Neta G, Glasgow RE, Carpenter CR, et al. A framework for enhancing the value of research for dissemination and implementation. *American Journal of Public Health* 2015; 105: 49-57

38. Colditz GA. The promise and challenges of dissemination and implementation research. In: Brownson RC, Colditz GA, Proctor EK. Dissemination and implementation research in health: Translating science to practice. 1st Edition. New York: Oxford University Press, 2012. 3-23
39. Chan A, Tetzlaff JM, Gøtzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013;346:e7586
40. Calvert M, Kyte D, Mercieca-Bebber R, et al. Guidelines for Inclusion of Patient-Reported Outcomes in Clinical Trial Protocols: The SPIRIT-PRO Extension. *JAMA*. 2018;319:483-94. doi:10.1001/jama.2017.21903 ** (Of considerable importance as best practice for outlining PRO items for inclusion in trial protocols)
41. EU. REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC. 2014. Available from: <http://www.hra.nhs.uk/resources/before-you-apply/types-of-study/clinical-trials-of-investigational-medicinal-products/clinical-trials-investigational-medicinal-products-ctimps-eu-legislation/> [Accessed: 01/11/17]
42. Calvert M, Blazeby J, Altman DG, et al. Reporting of Patient Reported Outcomes in Randomised Trials: the CONSORT PRO Extension. *JAMA*. 2013;309:814-22 ** (Of considerable importance as best practice for effective of reporting PRO content)
43. House of Lords Select Committee. Barrier to trade and security if data transfers are hindered after Brexit (2017). Available from: <https://www.parliament.uk/business/committees/committees-a-z/lords-select/eu-home-affairs-subcommittee/news-parliament-2017/data-protection-report-published/> [Accessed: 01.11.17]
44. Impact of Brexit on cancer care and research. *The Lancet Oncology* 2016; 17:539
45. Eurodis. Rare disease patient registries (2013). Available from: https://www.eurordis.org/sites/default/files/publications/Factsheet_registries.pdf [Accessed: 01.11.17]
46. Cancer Research UK. Cancer survival statistics (2017). Available from: <http://www.cancerresearchuk.org/health-professional/cancer-statistics/survival> [Accessed: 01/11/2017]
47. Fallowfield L, Nadler E, Gilloteau I. et al. Quality of survival: a new concept framework to assess the quality of prolonged life in cancer. *Expert Review of Quality of Life in Cancer Care*. 2017;2
48. Kotronoulas G, Kearney N, Maguire R, et al. What is the value of the routine use of patient-reported outcome measures toward improvement of patient outcomes, processes of care, and health service outcomes in cancer care? A systematic review of controlled trials. *Journal of Clinical Oncology*. 2014;32:1480-501
49. Velikova G, Booth L, Smith AB, et al. Measuring quality of life in routine oncology practice improves communication and patient wellbeing: a randomized controlled trial. *Journal of Clinical Oncology*. 2004;22:714-24
50. Gotay CC, Kawamoto CT, Bottomley A, et al. The prognostic significance of Patient-Reported Outcomes in cancer clinical trials. *Journal of Clinical Oncology*. 2008;26:1355-63
51. Efficace F, Bottomley A, Coens C. et al. Does a patient's self-reported health-related quality of life predict survival beyond key biomedical data in advanced colorectal cancer? *European Journal of Cancer*. 2006;42:42-9

52. Basch E, Deal AM, Dueck AC. et al. Overall survival results of a trial assessing patient-reported outcomes for symptom monitoring during routine cancer treatment. *JAMA*. 2017; 318:197-8
53. Sutherland HJ, Llewellyn-Thomas HA, Lockwood GA, et al. Cancer patients: Their desire for information and participation in treatment decisions. *J Royal Soc Med* 1989; 82: 260–263
54. Cassileth BR, Zupkis RV, Sutton-Smith K, et al. Information and participation preferences among cancer patients. *Ann Intern Med* 1980; 92: 832–6
55. Brundage M, Leis A, Bezjak A, et al. Cancer patients' preferences for communicating clinical trial quality of life information: a qualitative study. *Qual Life Res* 2003;12:395–404
56. Davison J, Degner LF, Morgan TR. Information and decision-making preferences of men with prostate cancer. *Oncol Nurs Forum* 1995; 22: 1401–8
57. Feldman-Stewart D, Brundage MD, Hayter C, et al. What questions do patients with curable prostate cancer want answered? *Med Decision Making* 2000; 20: 7–19
58. Søreide K, Søreide AH. Using Patient-Reported Outcome Measures for Improved Decision-Making in Patients with Gastrointestinal Cancer – the Last Clinical Frontier in Surgical Oncology? *Frontiers in Oncology*. 2013;3:157. doi:10.3389/fonc.2013.00157
59. Charles L, Bardes MD. Defining “Patient-Centered Medicine”. *N Engl J Med* 2012; 366:782-3
60. Srivastava R. Dealing with Uncertainty in a Time of Plenty. *N Engl J Med* 2011; 365:2252-3
61. Detmar SB, Muller MJ, Schornagel JH, et al. Health-related quality-of-life assessments and patient-physician communication: a randomized controlled trial. *JAMA*. 2002; 288: 3027-34
62. Baeksted C, Pappot H, Nissen A, et al. Feasibility and acceptability of electronic symptom surveillance with clinician feedback using the Patient-Reported Outcomes version of Common Terminology Criteria for Adverse Events (PRO-CTCAE) in Danish prostate cancer patients. *Journal of Patient-Reported Outcomes*.2017; 1:1 <https://doi.org/10.1186/s41687-017-0005-6>
63. Basch E, Deal AM, Dueck AC, et al. Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment. *JAMA*. 2017;318:197-8
64. Holch P, Warrington L, Bamforth LCA, et al. Development of an integrated electronic platform for patient self-report and management of adverse events during cancer treatment. *Annals of Oncology*. 2017; 28: 2305–11
65. Cancer Research UK. Taskforce report: achieving world-class cancer outcomes (2015). Available from: http://scienceblog.cancerresearchuk.org/2015/07/19/taskforce-report-achieving-world-class-cancer-outcomes/?utm_source=twitter_cr_uk&utm_medium=cruksocialmedia&utm_campaign=owntwitter_tweet/ [Accessed 02/11/2017]
66. NHS England. New quality of life measure for recovering cancer patients (2017). Available from: <https://www.england.nhs.uk/2017/09/new-quality-of-life-measure-for-recovering-cancer-patients/> [Accessed 02/11/2017]
67. Quality Health. National Cancer Patient Experience Survey: 2015 Reports. Available from: <http://www.ncpes.co.uk/index.php/reports/2015-reports> [Accessed 1/12/17]
68. Quality Health. National Cancer Patient Experience Survey 2016: National Results Summary. Available from: <http://www.ncpes.co.uk/index.php/reports/2016-reports/national-reports-1/3572-cpes-2016-national-report/file>. [Accessed 6.10.17]

69. NHS England. Achieving world-class cancer outcomes: Taking the strategy forward (2016). Available from: <https://www.england.nhs.uk/wp-content/uploads/2016/05/cancer-strategy.pdf>. [Accessed 6.10.17]
70. NHS England. Implementing the Cancer Taskforce recommendations: Commissioning person centred care for people affected by cancer (2016). Available from: <https://www.england.nhs.uk/wp-content/uploads/2016/04/cancer-guid-v1.pdf>. [Accessed 6.10.17]
71. Independent Cancer Taskforce. Achieving world-class cancer outcomes: A strategy for England 2015-2020 (2015). Available from: http://www.cancerresearchuk.org/sites/default/files/achieving_world-class_cancer_outcomes_-_a_strategy_for_england_2015-2020.pdf. [Accessed 6.10.17]
72. Basch, E. The Rise of Patient-Reported Outcomes in Oncology. ASCO Daily News. Available from: <https://am.asco.org/daily-news/rise-patient-reported-outcomes-oncology>. [Accessed 27.10.17]
73. Sellers L, Savas AN, Davdas R. et al, Patient-reported outcome measures in metastatic prostate cancer. Trends in Urology and Men's Health, 2016; 7: 28–32; DOI: 10.1002/tre.504
74. Bouazza YB, Chiari I, El Kharbouchi O, et al. Patient-reported outcome measures (PROMs) in the management of lung cancer: A systematic review. Lung Cancer 2017. 113: 140–51; <http://dx.doi.org/10.1016/j.lungcan.2017.09.011>
75. Rogers SN. Improving quality-of- life questionnaires in head and neck cancer, Expert Review of Quality of Life in Cancer Care. 2016: 61-71. <http://dx.doi.org/10.1080/23809000.2016.1142357>
76. Rogers SN, Barber B. Using PROMs to guide patients and practitioners through the head and neck cancer journey. Patient Related Outcome Measures. 2017;8: 133-142. DOI <https://doi.org/10.2147/PROM.S129012>
77. Weldring T, Smith, S; Article Commentary: Patient-Reported Outcomes (PROs) and Patient-Reported Outcome Measures (PROMs). Health Services Insights 2013;6 61–8 doi: 10.4137/HSI.S11093
78. Catt S, Starkings R, Shilling V, et al. Patient-reported outcome measures of the impact of cancer on patients' everyday lives: a systematic review. Journal of Cancer Survival 2017; 11:211–32 DOI 10.1007/s11764-016-0580-1
79. Howell D, Molloy S, Wilkinson K et al. Patient-reported outcomes in routine cancer clinical practice: a scoping review of use, impact on health outcomes, and implementation factors. Annals of Oncology 2015; 26: 1846–58, doi:10.1093/annonc/mdv181
80. Kirwan JR, Minnock P, Adebajo A, et al. Patient perspective: fatigue as a recommended patient-centred outcome measure in rheumatoid arthritis. J Rheumatol 2007; 34: 1174–7
81. Tugwell P, Bombardier C. A methodologic framework for developing and selecting endpoints in clinical trials. J Rheumatol 1982; 9: 758–62
82. Streiner D, Norman G. Health measurement scales: a practical guide to their development and use. Oxford: Oxford University Press; 1989
83. Bell MJ, Bombardier C, Tugwell P. Measurement of functional status, quality of life, and utility in rheumatoid arthritis. Arthritis Rheum 1990; 33: 591–601
84. Antunes B, Harding R, Higginson IJ. Implementing patient-reported outcome measures in palliative care clinical practice: A systematic review of facilitators and barriers. Palliative Medicine 2014; 28: 158–75; DOI: 10.1177/0269216313491619

85. Wild D, Grove A, Martin M, et al. Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: Report of the ISPOR Task Force for Translation and Cultural Adaptation. *Value in Health* 2005; 8: 94–104
86. Patrick DL, Burke LB, Gwaltney CJ et al; Content validity - Establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO good research practices task force report: Part 2 - Assessing respondent understanding. *Value in Health* 2011; 14: 978 –988
87. Reeve BB, Wyrwich KW, Wu AW et al. ISOQOL recommends minimum standards for patient-reported outcome measures used in patient-centered outcomes and comparative effectiveness research. *Quality of Life Research* 2013; 22:1889–905; DOI 10.1007/s11136-012-0344-y
88. Schultz KF, Altman DG, Moher D, et al. CONSORT 2010 Statement: Updated Guidelines for Reporting Parallel Group Randomized Trials. *Ann Intern Med.* 2010; 152:726-32. DOI: 10.7326/0003-4819-152-11-201006010-00232
89. Foster C, Haviland J, Winter J, et al. Pre-Surgery Depression and Confidence to Manage Problems Predict Recovery Trajectories of Health and Wellbeing in the First Two Years following Colorectal Cancer: Results from the CREW Cohort Study. *PLoS ONE* 2016; 11: e0155434. doi:10.1371/journal.pone.0155434 ** (Of considerable importance due to demonstration of value of quality of life as indicator of recovery)
90. Maher J, Velikova G, Betteley A. Incurable, but treatable: how to address challenges for an emerging group. *BMJ Supportive & Palliative Care* 2015;5:322–24. doi:10.1136/bmjspcare-2015-001047 * (Of importance due to emergence of new patient groups resulting from improved cancer survival).
91. Foster C, Calman L, Richardson A, et al. Improving the lives of people living with and beyond cancer: Generating the evidence needed to inform policy and practice. *Journal of Cancer Policy* 2018; <https://doi.org/10.1016/j.jcpo.2018.02.004>
92. Evans SM, Millar JL, Moore CM, et al. Cohort profile: the TrueNTH Global Registry - an international registry to monitor and improve localised prostate cancer health outcomes. *BMJ Open* 2017;7:e017006. doi:10.1136/bmjopen-2017-017006