

Making better use of existing cancer data: Patient Reported Outcomes and Behavioural Evidence: a new international initiative

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Keywords: cancer, quality of life, patient reported outcomes.

Cancer clinical trials have traditionally assessed clinical end points such as overall survival or progression-free survival. In more recent years, clinical investigators have started to include health-related quality of life (HRQOL) measures to better portray the effects of treatment (Bottomley 2002). This series of measures fall under the umbrella (as the USA Food and Drug Agency prefers) of a broader concept called patient-reported outcomes (Burke *et al.* 2008). The increasing number of publications reporting HRQOL research in recent years is evidence of this expanded view of clinical outcomes, but the inclusion of such information has been gradual. It is likely that the first HRQOL study in oncology was more than 50 years ago (Karnofsky *et al.* 1948). Lung cancer patients were given nitrogen mustard and clinicians then assessed patient functioning, using a rather crude, untested and unvalidated measure by today's standards (Bottomley 2008). Since that study, researchers have continued to

progressively develop more sophisticated approaches for looking at HRQOL outcomes, thus systematically improving both the collection and interpretation of HRQOL information. This has led to more reliable and interpretable results and an increase in the use of HRQOL assessment in cancer in general. Although HRQOL has helped to effectively interpret the overall results of many clinical trials, ground-breaking studies that alter clinical practice are infrequent. Published reports have used a variety of different HRQOL outcome measures, thus complicating our ability to draw inferences (e.g. by meta-analysis) across different data sets, varying treatment regimens or different cancer types.

With each passing year, it becomes more expensive to conduct clinical trials (Therasse 2005), and it is expected that the overall number of trials conducted in the European Union, including the conduct of HRQOL research, will decline, leaving HRQOL researchers with a plethora of unanswered questions. Therefore, it seems likely that we will have to re-examine data already collected in order to provide additional insight into the experience of cancer treatments.

One example of this approach is provided by an European Organisation for Research and Treatment of Cancer

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DOI: 10.1111/j.1365-2354.2009.01092.x

European Journal of Cancer Care, 2009, **18**, 105–107

(EORTC) international collaborative initiative, which aims to use existing data from multiple trials collected over many years across different countries. By integrating HRQOL data from over 10 000 patients collected in robust published randomised controlled trials, the EORTC is addressing key questions such as: Is the summary measure of HRQOL as captured by the EORTC QLQ-C30 tool or any of the 15 individual HRQOL parameters within the QLQ-C30 prognostic of survival? It is also addressing how different languages and cultures shape our understanding of HRQOL and affect the interpretations made from international HRQOL data sets. The initiative is also considering whether the presence of symptom clusters can provide additional prognostic information about the survival chances or well-being of cancer patients, new clinical end points and whether we can improve the utility of clinical trials by using different time windows for the collection and analysis of data thus obtained. In addition, the initiative is also investigating the extent of agreement between patient and clinician-assessed symptoms and how HRQOL varies for individual cancer patients across the cancer care continuum.

In considering such issues, we must identify the most robust statistical methods to analyse data derived from different clinical trial settings and create better interpretive and decision-making tools to guide clinicians in their decision making. We must also identify the best methods to gauge the significance of reported differences in trial data and use these measures when reporting HRQOL results. As a consequence of this, the EORTC international collaborative initiative will attempt to address these many unresolved issues over the next 2 years through an extensive analysis of existing EORTC data sets.

Thanks to a generous unrestricted academic grant from the Pfizer Foundation, the EORTC has been able to attract international experts across different fields within oncology to form the EORTC PROBE (Patient Reported Outcomes and Behavioural Evidence) Advisory Group. The main focus of PROBE will be to undertake detailed secondary analyses of existing psychosocial and clinical data to ensure that clinicians and researchers have a better grasp of HRQOL issues in cancer patients by addressing the many methodological and interpretive challenges they face using hypothesis-driven research questions.

Within the EORTC collaboration of 2500 clinicians, data from randomised controlled trials involving over 10 000 individual patients have been pooled together. This will provide us with a robust resource to address the above questions. As one challenge has been the inability to

compare data across different studies due to the use of different HRQOL tools, PROBE will provide a unique research opportunity, because all of the data in this international collaboration make use of the same EORTC QLQ-C30 questionnaire.

Furthermore, PROBE scientists believe that there is an opportunity to further expand the database by including data from organisations such as the United Kingdom's Medical Research Council and the National Cancer Institute of Canada's Clinical Trials Group. These long-standing EORTC partners have frequently used the EORTC QLQ-C30 tool in their randomised controlled trials, the Canadian group using it as their tool of choice for over 14 years, with over 14 000 patients providing data for their studies.

As individual studies have constraints in assessing HRQOL, the PROBE initiative could provide a solution by serving as a repository for high-quality clinical trial outcomes, allowing the sharing of existing data between clinical trial groups using the EORTC measurement system. This repository is likely to grow as other international groups are welcome to join this initiative, providing a possible means of addressing the many HRQOL questions not considered in smaller studies.

Many clinicians have expressed a need for further HRQOL training, however (Palmboom *et al.* 2007), and to address this need, the EORTC and PROBE have established a 3-day HRQOL training programme involving a faculty of 25 international key opinion leaders from across the globe (see <http://www.eortc.be/probe>). Attendance at this symposium is free of charge and will help physicians, nurses and other healthcare professionals better understand the opportunities and benefits of using HRQOL evidence in randomised controlled trials. It will make healthcare professionals aware of the key role they play in collecting data from patients and the potential applications of HRQOL data in offering the best possible care for cancer patients. In addition, in order to encourage young investigators and oncologists to become acquainted with HRQOL, PROBE is offering 20 travel fellowships to support attendance at the symposium, which we are promoting through different medical societies such as The International Society of Quality of Life Research and The European Journal of Cancer Care.

The wealth of HRQOL data and collaboration among international HRQOL experts will help the PROBE initiative to further develop the HRQOL research agenda. The PROBE team invites the participation of additional international groups by sharing data from hitherto closed randomised controlled trials that have used the EORTC QLQ-C30 to assess HRQOL. It is acknowledged that col-

laboration across many research institutions is likely to generate more HRQOL questions, but it will also generate answers that will eventually lead to a better understanding of HRQOL and ultimately to the enhanced care of cancer patients in the future.

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