Special Article

ASCPRO Recommendations for the Assessment of Fatigue as an Outcome in Clinical Trials

Andrea M. Barsevick, PhD, RN, FAAN, Charles S. Cleeland, PhD, Donald C. Manning, MD, PhD, Ann M. O'Mara, PhD, RN, FAAN, Bryce B. Reeve, PhD, Jane A. Scott, PhD, and Jeff A. Sloan, PhD

Fox Chase Cancer Center (A.M.B.), Philadelphia, Pennsylvania; The University of Texas M. D. Anderson Cancer Center (C.S.C.), Houston, Texas; Shionogi-USA Inc. (D.C.M.), Florham Park, New Jersey; National Cancer Institute (A.M.O., B.B.R.), Bethesda, Maryland; Mayo Clinic, Graduate School of Medicine (J.A.Sl.), Rochester, Minnesota, USA; and MAPI Values (J.A.Sc.), Research Director, Mapi Values, Adelphi Mill, Bollington, Macclesfield, Cheshire, United Kingdom

Abstract

Context. Development of pharmacological and behavioral interventions for cancer-related fatigue (CRF) requires adequate measures of this symptom. A guidance document from the Food and Drug Administration offers criteria for the formulation and evaluation of patient-reported outcome measures used in clinical trials to support drug or device labeling claims.

Methods. An independent working group, ASCPRO (Assessing Symptoms of Cancer Using Patient-Reported Outcomes), has begun developing recommendations for the measurement of symptoms in oncology clinical trials. The recommendations of the Fatigue Task Force for measurement of CRF are presented here.

Results. There was consensus that CRF could be measured effectively in clinical trials as the sensation of fatigue or tiredness, impact of fatigue/tiredness on usual functioning, or as both sensation and impact. The ASCPRO Fatigue Task Force constructed a definition and conceptual model to guide the measurement of CRF. ASCPRO recommendations do not endorse a specific fatigue measure but clarify how to evaluate and implement fatigue assessments in clinical studies. The selection of a CRF measure should be tailored to the goals of the research. Measurement issues related to various research environments were also discussed.

Conclusions. There exist in the literature good measures of CRF for clinical trials, with strong evidence of clarity and comprehensibility to patients, content and construct validity, reliability, and sensitivity to change in conditions in which

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Address correspondence to: Andrea M. Barsevick, PhD, RN, FAAN, Fox Chase Cancer Center, 333 Cottman Avenue, Philadelphia PA 19111, USA. E-mail: andrea.barsevick@fccc.edu

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one would expect them to change (assay sensitivity), and sufficient evidence to establish guides for interpreting changes in scores. Direction for future research is discussed. J Pain Symptom Manage 2010;39:1086–1099.

Key Words
Cancer-related fatigue, self-report measures, clinical trials, patient-reported outcomes

Introduction

Fatigue is the most common and distressing symptom related to cancer and its treatment.[1] Prevalence estimates of cancer-related fatigue (CRF) during treatment range from 25% to 99%, depending on the sample and method of assessment.[2] This symptom may be present at diagnosis, during treatment, chronically for some survivors, and/or at the end of life. CRF is known to affect quality of life; functional outcomes, including work; and, possibly, survival. Fatigue is distinct from many other cancer-related symptoms because it is *not* unique to cancer or its treatment. Almost everyone experiences fatigue every day, blurring the line between the normal occurrence of fatigue and the pathological symptom of CRF. Despite a large body of research that has shed light on the problem of CRF and its management, there are gaps in our scientific understanding of this symptom.

Although hundreds of thousands of cancer patients are faced with debilitating CRF at various stages in their illness, research into the efficacy of existing treatments and development of new treatments to reduce CRF has been slow. A major reason for lack of progress in this area has been the lack of consensus about how to conceptually define and measure CRF in clinical research. In contrast to other cancer-related symptoms, such as pain or nausea/vomiting, where conceptual definitions are almost intuitive and measurement strategies are more established, unresolved issues regarding the definition and measurement of CRF have been a major impediment to progress in establishing the most effective treatments to manage it.

Perfect and final conceptualization and measurement of CRF is not a realistic goal. However, progress is needed, so that the people most at risk for CRF are not deprived of the benefits of new treatments that could relieve, minimize, or prevent the suffering associated with it. This need must be balanced against the danger of inaccurate or unclear understanding of CRF and the approval and use of inappropriate treatments for this symptom. In this article, the authors address the tension between the goal of scientific rigor and the need for a realistic approach in measuring CRF; recommendations will be made for resolving this.

In 2006, clinical researchers from academia and the pharmaceutical industry joined with participants and observers from government agencies to address symptom measurement issues related to clinical trials in cancer. This group—Assessing the Symptoms of Cancer using Patient-Reported Outcomes (ASCPRO)[3]—has the goal of developing recommendations for symptom measurement that promote clinical research focused on cancer-related symptoms. The formation of ASCPRO was, in part, a response to the issuance of guidance by the U.S. Food and Drug Administration (FDA) about the use of patient-reported outcomes in labeling claims.[4] The finalized guidance provides advice to the pharmaceutical industry about what the FDA will look for in review of patient-reported outcomes, including symptom reports, to ensure adequate development, validity, reliability, and interpretability of these outcomes for regulatory decision making about the safety and efficacy of treatments. Although the FDA guidance document is binding only to research conducted in support of labeling claims, the authors address some issues raised in the document that are also relevant to the broader academic and clinical research communities.

ASCPRO is indebted to the preceding efforts of the international networking groups, Outcome Measures in Rheumatology[5] and the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials.[6] These groups sought to improve the conceptualization and