Patient versus clinician symptom reporting using the National Cancer Institute Common Terminology Criteria for Adverse Events: results of a questionnaire-based study

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Summary

Background **The Common Terminology Criteria for Adverse Events (CTCAE) are used as standard practice in trials of cancer treatments by clinicians to elicit and report toxic effects. Alternatively, patients could report this information directly as patient-reported outcomes, but the accuracy of these reports compared with clinician reports remains unclear. We aimed to compare the reporting of symptom severity reported by patients and clinicians.**

Methods **Between March and May, 2005, a questionnaire with 11 common CTCAE symptoms was given to consecutive outpatients and their clinicians (physicians and nurses) in lung and genitourinary cancer clinics in the Memorial Sloan-Kettering Cancer Center, New York, NY, USA. Patients completed a version that used language adapted from the CTCAE for patient self-reporting. The results from the questionnaire were compared with clinician reporting of the same symptoms.**

Findings **Of 435 patients and their clinicians asked to take part in the study, 400 paired surveys were completed. For most symptoms, agreement between patient and clinician was high, and most discrepancies were within a grade difference of one point. Agreement was higher for symptoms that could be observable directly, such as vomiting and diarrhoea, than for more subjective symptoms, such as fatigue and dyspnoea. Differences in symptom reporting rarely would have changed treatment decisions or dosing, and patients assigned greater severity to symptoms more than did clinicians. No significant differences were recorded between the results when the questionnaire was completed by the patient before or after the clinician.**

Interpretation **Patient reporting of symptoms could add to the current approach to symptom monitoring in cancer treatment trials. Future research should assess the effect of self reporting on clinical outcomes and efficiency, and the use of real-time collection of patient-reported outcomes for early detection of potentially serious adverse events.**

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Introduction

Monitoring of adverse events is standard in trials that assess new cancer drugs, indications for drugs, or treatment combinations (ie, cancer treatment trials).[1] In the USA, the mandated instrument for this purpose is the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE).[2] The CTCAE includes items derived from measured objective factors, analytical tests, and the patient's subjective experience (ie, symptoms),[3] all of which are currently reported by clinicians. Clinical staff obtain, interpret, and report patient symptoms, a process that can be cumbersome and susceptible to data degradation (ie, transcription errors, omissions). In practice, symptoms are abstracted by research support staff members on the basis of their review of the written medical record. An alternative approach—the direct collection of patient-reported outcomes—is standard in other settings, such as the measurement of health-related quality-of-life[4–6] and symptom research,[7–10] but has not been adopted to monitor toxicity symptoms in cancer treatment trials. Interest in the use of self-reported symptoms as potential sources of information on clinical trial outcomes and toxic effect data has increased in investigators, regulatory agencies, and industry sponsors.[4,11,12] Although the CTCAE is widely familiar to oncology investigators and health professionals, most patients are not familiar with this scale or its details.

We have developed a version of the CTCAE that uses language suitable for patients and is designed for online self-reporting during chemotherapy.[13] This version showed high levels of patient use and satisfaction, and of clinician acceptance. However, patient responses to the CTCAE have not been compared with the current standard of clinician reporting. Past comparisons of patient versus clinician assessments of health-related quality-of-life have shown variable results,[14–17] with suggestions from symptom research that clinicians report fewer symptoms[10,18] of lower severity[8,9] than patients. We aimed to compare the reporting of symptom severity for a set of symptoms commonly assessed during cancer treatment trials between patients and clinicians.

Methods

Participants and procedures

Consecutive outpatients were approached by a research assistant (TM) to complete the questionnaire in the waiting areas of the thoracic and genitourinary clinics of the

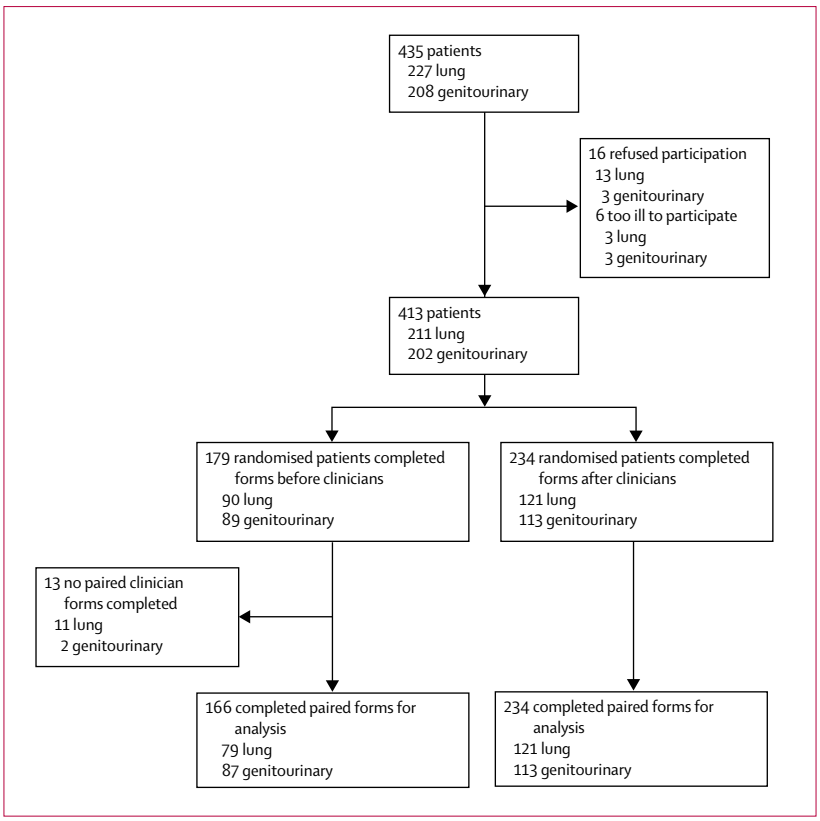

Figure 1: **Patient and clinician participation**

See Online for webtable

Memorial Sloan-Kettering Cancer Center, New York, NY, USA. No restrictions were placed on disease stage or type of treatment, although patients needed to read and understand English. Every patient could complete only one questionnaire. Every questionnaire contained items for seven core symptoms, two lung-specific symptoms, and two genitourinary-specific symptoms. No specific assistance was provided to patients at the time of completion of the questionnaire, but the research assistant was available to answer questions of clarification. Basic demographic information (ie, age, sex, cancer type and stage, treatment type, and routine care *vs* clinical trial enrollee) was obtained for all patients. Institutional review by the Memorial Sloan-Kettering Institutional Review Board established that the design of this study and the information obtained did not pose a large risk to the safety of patients or to the security of protected health information.

For every patient participant, the clinician who assessed the patient as a part of the scheduled visit was asked to complete a paired clinician questionnaire at the time of the appointment. Questionnaires were collected immediately after the visit. Every patient–clinician questionnaire pair was assigned a tracking number for analysis. Clinicians and patients were not given access to each others' responses, and if more than one clinician interviewed a patient, only the first clinician was asked to complete the questionnaire.

The questionnaire was developed by the use of items in the CTCAE (version 3.0). Items were transcribed unchanged for a clinician version of the questionnaire, and the patient version included identical items with syntactical modifications to improve patient comprehension. CTCAE items are generally graded on an ordinal scale of 1–5, but grade 5 toxic effects (ie, death) were not included in our questionnaire. The original clinician language and adapted patient language for the selected CTCAE items are shown in the webtable. Instructions were included at the top of each questionnaire and specified the reporting period for symptoms, in accordance with the National Cancer Institute guidelines for the CTCAE: "If you are receiving chemotherapy, please report the worst your symptoms have been since your last treatment. If you are not receiving chemotherapy, please report the worst your symptoms have been since your last clinic visit".

A core set of symptoms that were known to be easily identifiable in patients with cancer given cytotoxic chemotherapy irrespective of the type of cancer was included in both the lung and genitourinary questionnaires: anorexia, constipation, diarrhoea, fatigue, nausea, pain, and vomiting (items 1–7 in the webtable). Disease-specific items relevant to lung cancer (ie, cough and dyspnoea) were added to the lung questionnaire, and items appropriate to genitourinary malignant diseases (ie, urinary frequency and hot flushes) were added to the genitourinary questionnaire (items 8a–9a and 8b–9b, respectively, in webtable).

Statistical analysis

For all symptoms, we measured the proportion of pairs for which clinicians and patients gave an identical grade. We then measured the proportion of pairs that disagreed for each symptom by one point (eg, patient grade 2 and clinician grade 1), and the proportion that disagreed by two or more points (eg, patient grade 2 and clinician grade 4). We also tabulated the number of symptoms for which each pair agreed (eg, absolute agreement for three symptoms and disagreement for six symptoms).

Kappa and weighted kappa values were calculated as a measure of agreement between pairs for each symptom by the use of Cicchetti-Allison coefficient weights for weighted kappas.[19] In this model, a kappa value less than 0·4 suggests poor agreement, 0·4–0·75 implies fair-to-good agreement, and 0·75 or more suggests excellent agreement. Because this approach has been criticised,[20–22] especially for analyses of ordinal data with asymmetry in the directionality of scoring differences,[23] we also dichotomised symptom grades into non-serious (<2) and serious (≥3) categories, a delineation chosen because grades 3 or more are reportable and can be grounds to hold or reduce the dose of treatment.[9] McNemar's exact test was used to test for marginal homogeneity, where $p<0·05$ indicated significant differences in grading between pairs (ie, poor agreement).