

# Letters

## RESEARCH LETTER

### Overall Survival Results of a Trial Assessing Patient-Reported Outcomes for Symptom Monitoring During Routine Cancer Treatment

Symptoms are common among patients receiving treatment for advanced cancers,<sup>1</sup> yet are undetected by clinicians up to half the time.<sup>2</sup> There is growing interest in integrating electronic patient-reported outcomes (PROs) into routine oncology practice for symptom monitoring, but evidence demonstrating clinical benefit has been limited.<sup>3</sup>

We assessed overall survival associated with electronic patient-reported symptom monitoring vs usual care based on follow-up from a randomized clinical trial.<sup>4</sup>

**Methods** | The study was approved by the Memorial Sloan Kettering institutional review board and written informed consent was obtained from participants. Consecutive patients initiating routine chemotherapy for metastatic solid tumors at Memorial Sloan Kettering Cancer Center in New York between September 2007 and January 2011 were invited to participate in a randomized clinical trial. Participants were randomly assigned either to the usual care group or to the PRO group, in which patients provided self-report of 12 common symptoms from the National Cancer Institute's Common Terminology Criteria for Adverse Events at and between visits via a web-based PRO questionnaire platform. Participation was continuous until cessation of cancer treatment, voluntary withdrawal from the trial, transition to hospice care, or death.

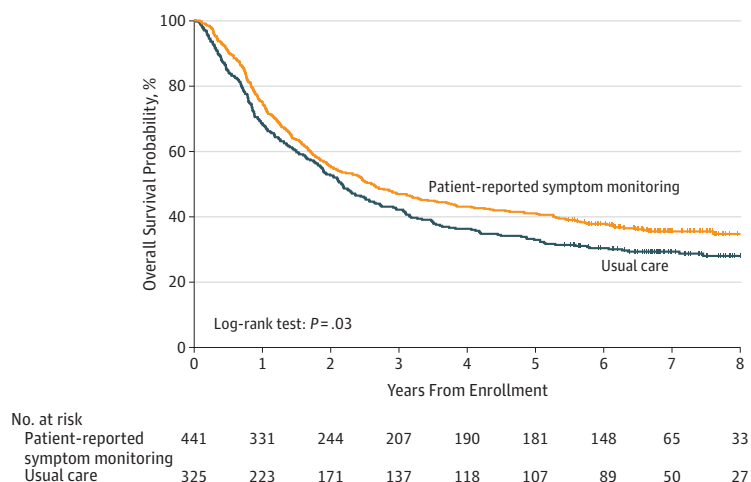
When the PRO group participants reported a severe or worsening symptom, an email alert was triggered to a clinical nurse responsible for the care of that patient.

A report profiling each participant's symptom burden history was generated at clinic visits for the treating oncologist. The usual care group received the standard procedure for monitoring symptoms in oncology practice: symptoms were discussed during clinical encounters, and patients could contact the office by telephone between visits for concerning symptoms.

The protocol-specified primary outcome was change in health-related quality of life at 6 months compared with enrollment and was the basis of the sample size determination.<sup>4</sup> Significant benefits in quality of life as well as secondary outcomes of 1-year quality-adjusted survival (mean: 8.7 months in the PRO group vs 8.0 months in the usual care group;  $P = .004$ ), duration of chemotherapy, and emergency department use were found and previously reported.<sup>4</sup> A post hoc decision to analyze overall survival was made prior to data analysis. Mortality was verified from the National Death Index. Overall survival was estimated using the Kaplan-Meier method and compared between groups using a log-rank test and Cox proportional hazards regression adjusting for age, sex, race, education level, level of prior computer use, and primary cancer type. All analyses were conducted using SAS (SAS Institute), version 9.4, and testing was 2-sided with  $P$  values less than .05 considered significant.

**Results** | Of 766 patients randomized, the median age was 61 years (range, 26-91), 86% were white, 58% women, 22% had less than a high school education, and 30% were computer inexperienced, as reported.<sup>4</sup> Baseline variables were well balanced between study groups.

Figure. Overall Survival Among Patients With Metastatic Cancer Assigned to Electronic Patient-Reported Symptom Monitoring During Routine Chemotherapy vs Usual Care



Crosses indicate censored observations. Enrollment in the patient-reported symptom monitoring group was enriched for a preplanned subgroup with low baseline computer experience as part of a feasibility substudy with a 2:1 randomization ratio in that subgroup (N = 227) and a 1:1 ratio in the computer-experienced subgroup (N = 539), yielding 441 participants in the patient-reported symptom monitoring group, and 325 in the usual care group. With a minimum follow-up of 5.4 years, median follow-up was 6.9 years (interquartile range, 6.5-7.7) for the electronic patient-reported symptom monitoring group and 7 years (interquartile range, 6.6-8.1) for the usual care group.

Overall survival was assessed in June 2016 after 517 of 766 participants (67%) had died, at which time the median follow-up was 7 years (interquartile range, 6.5-7.8). Median overall survival was 31.2 months (95% CI, 24.5-39.6) in the PRO group and 26.0 months (95% CI, 22.1-30.9) in the usual care group (difference, 5 months;  $P = .03$ ) (Figure). In the multivariable model, results remained statistically significant with a hazard ratio of 0.83 (95% CI, 0.70-0.99;  $P = .04$ ).

**Discussion |** Integration of PROs into the routine care of patients with metastatic cancer was associated with increased survival compared with usual care. One potential mechanism of action is early responsiveness to patient symptoms preventing adverse downstream consequences. Nurses responded to symptom alerts 77% of the time with discrete clinical interventions including calls to provide symptom management counseling, supportive medications, chemotherapy dose modifications, and referrals.<sup>4</sup> Another potential mechanism is that patients in the intervention group were able to tolerate continuation of chemotherapy longer than usual care (mean, 8.2 months in the PRO group vs 6.3 months in the usual care group; difference, 1.9 months [95% CI, 0.7-3.0];  $P = .002$ ).<sup>4</sup>

Limitations of this study include conduct at a single tertiary care cancer center, although 14% of participants were non-white and 22% had an educational level of high school or less. The overall survival analysis was not prespecified, although the decision to conduct this evaluation was made prior to data analysis.

Electronic patient-reported symptom monitoring may be considered for implementation as a part of high-quality cancer care.

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**Acquisition, analysis, or interpretation of data:** All authors.

**Drafting of the manuscript:** Basch, Deal, Scher.

**Critical revision of the manuscript for important intellectual content:** All authors.

**Statistical analysis:** Deal, Dueck, Schrag.

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## COMMENT & RESPONSE

### Vaginal Fetal Fibronectin to Predict Spontaneous Preterm Birth

**To the Editor** Dr Esplin and colleagues assessed the accuracy of vaginal fetal fibronectin testing and cervical length for predicting spontaneous preterm birth in asymptomatic nulliparous women.<sup>1</sup> However, the manner in which fetal fibronectin testing was performed in the study raises concerns about the authors' conclusion that fetal fibronectin does not reliably predict spontaneous preterm birth in this population. On the contrary, when used as directed, the weight of evidence supports the use of fetal fibronectin testing both in women at risk of spontaneous preterm birth and in those who are asymptomatic.<sup>2,3</sup>

As acknowledged by Esplin and colleagues, one of the study's primary limitations was that the fetal fibronectin samples were self-collected by study participants using a swab inserted only 2 inches into the vagina. Hologic, the manufacturer of the fetal fibronectin immunoassay used in the study, does not support the self-collection of samples because it is