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Differential Effects of an Electronic Symptom Monitoring Intervention Based on the Age of Patients with Advanced Cancer

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Abstract

Background: Symptom monitoring interventions enhance patient outcomes, including quality of life (QOL), healthcare utilization, and survival, but it remains unclear whether older and younger patients with cancer derive similar benefits. We explored whether age moderates the improved outcomes seen with an outpatient electronic symptom monitoring intervention.

Patients and methods: We performed a secondary analysis of data from a randomized trial of 766 patients receiving chemotherapy for metastatic solid tumors. Patients received an electronic symptom monitoring intervention integrated with oncology care or usual oncology care alone. The intervention consisted of patients reporting their symptoms, which were provided to their physicians at clinic visits, and nurses received alerts for severe/worsening symptoms. We used regression models to determine if age (older or younger than 70 years) moderated the effects of the

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intervention on QOL (EuroQol EQ-5D), emergency room (ER) visits, hospitalizations, and survival outcomes.

Results: Enrollment rates for younger (589/777=75.8%) and older (177/230=77.0%) patients did not differ. Older patients (median age=75, range 70–91) were more likely to have an education level of high school or less (26.6% vs 20.9%, $p=0.029$) and to be computer-inexperienced (50.3% vs 23.4%, $p<0.001$) compared with younger patients (median age=58, range 26–69). Younger patients receiving the symptom monitoring intervention experienced lower risk for ER visits (hazard-ratio=0.74, $p=0.011$) and improved survival (hazard-ratio=0.76, $p=0.011$) compared with younger patients receiving usual care. However, older patients did not experience significantly lower risk for ER visits (hazard-ratio=0.90, $p=0.613$) or improved survival (hazard-ratio=1.06, $p=0.753$) with the intervention. We found no moderation effects based on age for QOL and risk of hospitalizations.

Conclusion: Among patients with advanced cancer, age moderated the effects of an electronic symptom monitoring intervention on the risk of ER visits and survival, but not QOL. Symptom monitoring interventions may need to be tailored to the unique needs of older adults with cancer.

Keywords

Symptoms; Quality of Life; Advanced Cancer; Geriatric Oncology; Outcomes Research; Hospitalization

Introduction

Studies demonstrate that integrating electronic patient-reported symptom monitoring into oncology care can help to improve patients' symptom burden, quality of life (QOL), healthcare utilization, and survival outcomes.[1–4] Based on this evidence, many centers have begun integrating electronic symptom monitoring with patient-reported outcomes into routine oncology care.[5] However, we currently lack studies describing the use and benefits of electronic symptom monitoring interventions for the geriatric oncology population.

Older adults with cancer represent the largest group of oncology patients, and these individuals possess unique care needs.[6, 7] Older patients frequently experience a distinct symptom burden and greater risk of chemotherapy toxicity than younger patients.[8–10] When caring for the geriatric oncology population, clinicians often encounter a complex constellation of issues needing to be addressed, such as impaired physical and cognitive function, concurrent comorbid conditions, increased risk of polypharmacy, and limited psychosocial support.[10–13] Thus, oncologists face challenges when trying to address all the multifaceted concerns of older patients with cancer during time-limited clinic visits, thereby leading to under-recognition of these patients' symptoms.[14] Consequently, electronic symptom monitoring interventions represent a promising solution to ensure clinicians consistently and efficiently assess older patients' symptoms, yet studies focused on such interventions in the geriatric oncology population are lacking.[15] Moreover, symptom monitoring interventions often require patients to report their symptoms electronically, potentially creating a barrier for less technologically-adept older individuals.[16, 17] Additionally, prior work suggests differential effects of supportive care

interventions between older and younger patients, but this has not been studied in symptom monitoring interventions.[18, 19] Therefore, studies are needed to investigate the willingness of older patients to participate in trials of electronic symptom monitoring, while also exploring whether age moderates the improved outcomes seen with these interventions.

In the current study, we sought to investigate differences by age regarding study enrollment and outcomes in a randomized trial of electronic patient-reported symptom monitoring. By comparing rates of study enrollment between older and younger patients, we hope to better understand the willingness of older adults with cancer to participate in a trial of electronic patient-reported symptom monitoring. We also sought to explore whether age moderates the effects of an electronic symptom monitoring intervention on patients' QOL, healthcare utilization, and survival outcomes. By investigating the differential effects of electronic symptom monitoring based on patients' age, this study will inform future efforts seeking to integrate electronic patient-reported outcomes into routine cancer care for the rapidly growing geriatric oncology population.

Methods

Study Design

We conducted a secondary, exploratory analysis of data collected from a randomized trial of electronic patient-reported symptom monitoring versus usual oncology care.[1, 2] The study procedures have been previously described, but briefly, we randomly assigned patients initiating chemotherapy for metastatic cancer to receive the electronic symptom monitoring intervention or usual oncology care alone.

Patients assigned to the symptom monitoring intervention self-reported 12 symptoms, selected because they are commonly-experienced during treatment and frequently impact the patient experience, via a web-based platform using questions adapted from the National Cancer Institute's Common Terminology Criteria for Adverse Events (graded from 0 [not present] to 4 [disabling]).[1] If an intervention patient reported a worsening (2 points) or severe (absolute grade 3) symptom, an e-mail alert was triggered to a clinical nurse responsible for the patient. After hours, participants were encouraged to call the office for concerning symptoms. The treating oncologist also received a report detailing patients' symptoms at each clinic visit. For the study, clinicians did not receive specific guidance about symptom management.

Patients assigned to the usual care group received the standard-of-care for symptom monitoring in oncology practice, in which patients discuss their symptoms with their clinician(s) during clinical encounters and contact the office between visits for concerning symptoms. Participation was continuous until discontinuing cancer treatment, voluntary withdrawal, or death. The Memorial Sloan Kettering Cancer Center (MSK) and Dana-Farber/Harvard Cancer Center institutional review boards determined that the current secondary study was exempt and did not meet the definition of human-subjects research.

Patient Selection

For the parent trial, 766 consecutive patients initiating chemotherapy for metastatic breast, genitourinary, gynecologic, or lung cancers enrolled at MSK in New York from September 2007 to January 2011. Patients were required to receive their chemotherapy at MSK and be able to read English. We excluded patients if they were participating in an investigational treatment study, as these studies often require symptom reporting for all patients.

Outcome Measures

In the parent trial, change in QOL from baseline to 6-months was the primary outcome. We evaluated patients' QOL using the EuroQol EQ-5D Index.[20] The EQ-5D Index assesses patients' QOL across five domains (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and produces a composite score between 0–1, with lower scores representing worse QOL. To investigate the impact of the intervention on healthcare utilization, we determined time to first emergency room (ER) visit and time to first hospitalization at MSK using data in the medical record.[1] To examine the effects of the intervention on overall survival, we obtained mortality data from the National Death Index. [2] We investigated time from study enrollment to death, censoring patients who had not died at the date of last follow-up.

Statistical Analysis

We used descriptive statistics to describe patient demographics and study variables, comparing younger and older patients (<70 versus ≥70 years at enrollment). We used an age cutoff of ≥70 years for subgroup analyses, as many studies use this cutoff when examining an older population.[13, 16] We ran an exploratory Subpopulation Treatment Effect Pattern Plot (STEPP) analysis, which confirmed age ≥70 years as an appropriate cut-point for our analyses(Supplemental-Figure-1). The STEPP approach allows investigators to explore the heterogeneity of treatment effects on outcomes across values of a continuous variable (e.g. patient age).[21] We chose the outcomes of QOL, healthcare utilization, and survival, as prior work demonstrated that this intervention had beneficial effects on these outcomes.[1, 2] To assess the degree to which patients' age moderated the effects of electronic symptom monitoring on QOL (EQ-5D Index mean change scores from baseline to 6-months), healthcare utilization (time to first ER visit and time to first hospitalization), and overall survival (time to death), we computed separate regression models for each outcome that included the following independent variables: group assignment, the moderating variable (age), and an interaction term between group assignment and the moderating variable. We considered interaction terms with $p < 0.15$ to indicate potential moderation worth exploring in subsequent subgroup analyses.[22, 23] We then used competing risk regression (with death treated as a competing event) and Cox proportional hazards regression to determine the effects of electronic symptom monitoring on time to first ER visit and overall survival, respectively, within the age subgroups. Consistent with prior publications of this trial, we adjusted regression models for patient sex, cancer type, race, education level, and computer experience.[1, 2] To help illustrate these findings, we compared the effects of electronic symptom monitoring on time to first ER visit and overall survival between study groups by age using the Kaplan-Meier method.

Results

Participant Sample

With 766 patients enrolled in the parent trial, we found no significant differences in the enrollment rates (enrolled/approached) for younger (589/777, 75.8%) and older (177/230, 77.0%) patients (Supplemental Figure-2). Younger patients had a median age of 58 years (range 26–69) and older patients had a median age of 75 years (range 70–91) (Table 1). When comparing differences in baseline characteristics by age, older patients were more likely to be male (73.5% vs 32.6%, $p < 0.001$), have a genitourinary cancer type (68.9% vs 20.9%, $p < 0.001$), education level of high school or less (26.6% vs 20.9%, $p = 0.029$), and to be computer-inexperienced (50.3% vs 23.4%, $p < 0.001$). We did not find a significant difference in the proportion of participants assigned to the usual care or intervention group in the older or younger subgroups. Similarly, baseline QOL scores did not differ between older and younger patients.

Outcomes by Age

Using linear regression, we found that patients' age did not moderate the effects of electronic symptom monitoring on QOL (age \times group assignment, $B = -0.02$, $SE = 3.42$, $p = 0.994$) or time to first hospitalization (age \times group assignment, $HR = 0.23$, $SE = 0.22$, $p = 0.304$). However, patients' age did appear to moderate the effects of electronic symptom monitoring on time to first ER visit (age \times group assignment, $HR = 0.35$, $SE = 0.24$, $p = 0.148$) and overall survival (age \times group assignment, $HR = 0.42$, $SE = 0.20$, $p = 0.034$).

Subsequent subgroup analyses by age (Table 2) showed that, among younger patients (age < 70 years), the electronic symptom monitoring intervention significantly reduced the hazard for time to ER visit ($HR = 0.74$, $SE = 0.12$, $p = 0.011$) but had no significant effect on this outcome for older patients ($HR = 0.90$, $SE = 0.22$, $p = 0.613$). As illustrated in Figure 1, the incidence of patients visiting the ER was significantly lower in the intervention arm compared with the usual care arm for the younger patients (median time to ER visit: 50.73 months vs 21.72 months, Gray's test p -value = 0.016), yet the difference seen between the intervention and usual care groups was not significant for the older patients (median time to ER visit: 17.61 months vs 21.98 months, Gray's test p -value = 0.738).

Additionally, we observed a significant moderation effect by age on overall survival, and subsequent subgroup analyses revealed that the electronic symptom monitoring intervention led to decreased hazard for death ($HR = 0.76$, $SE = 0.11$, $p = 0.011$) among younger patients. However, we did not find significant survival benefits for patients assigned to the intervention among the older patients ($HR = 1.06$, $SE = 0.17$, $p = 0.753$). Figure 2 illustrates that younger patients assigned to the electronic symptom monitoring intervention experienced significantly longer median overall survival compared with younger patients assigned to usual care (46.23 vs 30.14 months, log-rank p -value = 0.004), whereas we found no significant differences between intervention and usual care for the older patients (15.57 vs 12.94, log-rank p -value = 0.512).

Discussion

In this exploratory analysis of data from a randomized trial assessing the impact of an electronic symptom monitoring intervention among patients with advanced cancer, we demonstrated that age moderated some of the benefits derived from the intervention. We found that patients' age moderated the effects of electronic symptom monitoring on time to first ER visit and overall survival. Specifically, younger patients assigned to the electronic symptom monitoring intervention had lower risk for ER visits and better overall survival than younger patients assigned to usual care, yet older patients did not experience these intervention effects. Collectively, these findings suggest the potential for differential effects of electronic symptom monitoring based on patients' age.

To our knowledge, this is the first study to report that the effects of electronic symptom monitoring differ based on the age of patients with cancer. We found that an electronic symptom monitoring intervention helped younger patients with regards to their risk of ER visits and overall survival, but these benefits were not significant for older patients. Potentially, older patients did not derive benefits in terms of ER visits and survival due to the constellation of factors that may influence these outcomes in older adults with cancer, such as mobility, cognitive function, and the availability of social supports, which are not comprehensively addressed with a symptom monitoring intervention.[11, 12] We also found that older patients in our study were more likely to be computer-inexperienced, which could theoretically influence their experience with this type of intervention.[15, 16] However, prior work demonstrated that the benefits of this symptom monitoring intervention were greater for participants with limited computer experience.[1] Importantly, we did not find that age moderated the impact of electronic symptom monitoring on patients' QOL, thereby suggesting that older and younger patients both experienced significant QOL benefits from this intervention. These findings underscore that when investigating supportive care interventions for the geriatric cancer population, researchers should consider outcomes that are important to older adults, such as QOL, functional independence, and treatment tolerability.[24, 25] Thus, our findings are hypothesis-generating and additional work is needed to confirm the results and help us fully understand the mechanisms underlying the differential benefits of symptom monitoring interventions for younger and older patients with cancer.

Notably, older patients in our study were equally as likely to enroll in this randomized trial as their younger counterparts, which highlights their willingness to participate in a trial testing an electronic symptom monitoring intervention. Although cancer disproportionately impacts older adults, little research has sought to test age-specific interventions focused on the supportive care needs of the geriatric oncology population. The population of aging individuals is expected to continue to rise exponentially, and therefore it is imperative to design models of oncology care tailored to the complex needs of older adults with cancer.[6, 7] Additionally, we need more supportive care trials that enroll older individuals, thereby providing more age-diversity, and fostering investigations exploring differential effects between older and younger patients. Ultimately, additional research is needed to allow us to understand how best to develop interventions targeting the geriatric oncology population.

Our work underscores the need to study age as a moderator of intervention effects in supportive care trials. Prior research has demonstrated that older and younger patients have differing supportive care needs,[18, 19] yet studies had not yet shown that the impact of electronic symptom monitoring interventions differentially vary by age among patients with cancer. Understanding differential effects of interventions on younger versus older patients can be informative in: (1) enhancing current models of care by highlighting where existing standards of care may not address all the unique concerns of certain subgroups of patients; (2) developing innovative care models personalized to patients' distinct care needs; and (3) designing age-specific interventions for the geriatric oncology population to enhance care delivery and outcomes for this largest subgroup of patients with cancer. By demonstrating differential effects of electronic symptom monitoring based on patients' age, this work supports the need for population-specific interventions tailored to older individuals with cancer and should inform future efforts to support these patients with complex and diverse needs.

Our study has several limitations. First, this was an exploratory analysis, with a relatively modest sample size, and thus our hypothesis-generating findings merit confirmation in follow-up studies. Second, we only investigated moderation based on patient age, and future prospective studies should test the differential effects of electronic symptom monitoring interventions across other patient characteristics. Notably, we observed differences in the sexes and cancer types between older and younger patients in this study, and although we adjusted for this in our regression models, unmeasured confounding could still affect our findings. Third, our study sample included patients initiating treatment for advanced solid tumors at a tertiary cancer center, which limits our ability to generalize findings to patients outside of this population and care setting. Fourth, the current analysis was limited to QOL, healthcare utilization, and survival outcomes, and thus we lack information about potential differential effects on other important outcomes, such as patients' symptoms, physical function, and treatment tolerance. In addition, we cannot account for potentially important unmeasured confounds, including comorbid conditions, cognitive function, and social support.

In summary, we demonstrated differential effects of an electronic symptom monitoring intervention based on patient age regarding the risk of ER visits and survival, but not QOL. Specifically, we found that younger patients receiving electronic symptom monitoring experienced fewer ER visits and longer survival than those receiving usual care. Conversely, older patients did not experience these same benefits with electronic symptom monitoring. Thus, symptom monitoring interventions may need to be tailored to patients' age-specific care needs. Expanding on this work, future studies should seek to develop strategies for tailoring and personalizing symptom monitoring interventions to the individual supportive care needs of all patients with advanced cancer.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key Message:

In this analysis of randomized trial data, age moderated the impact of electronic symptom monitoring on patients' risk of emergency room (ER) visits and survival, but not quality of life. Younger patients receiving the intervention had lower risk of ER visits and improved survival compared to younger patients receiving usual care, yet older patients did not experience these intervention effects.

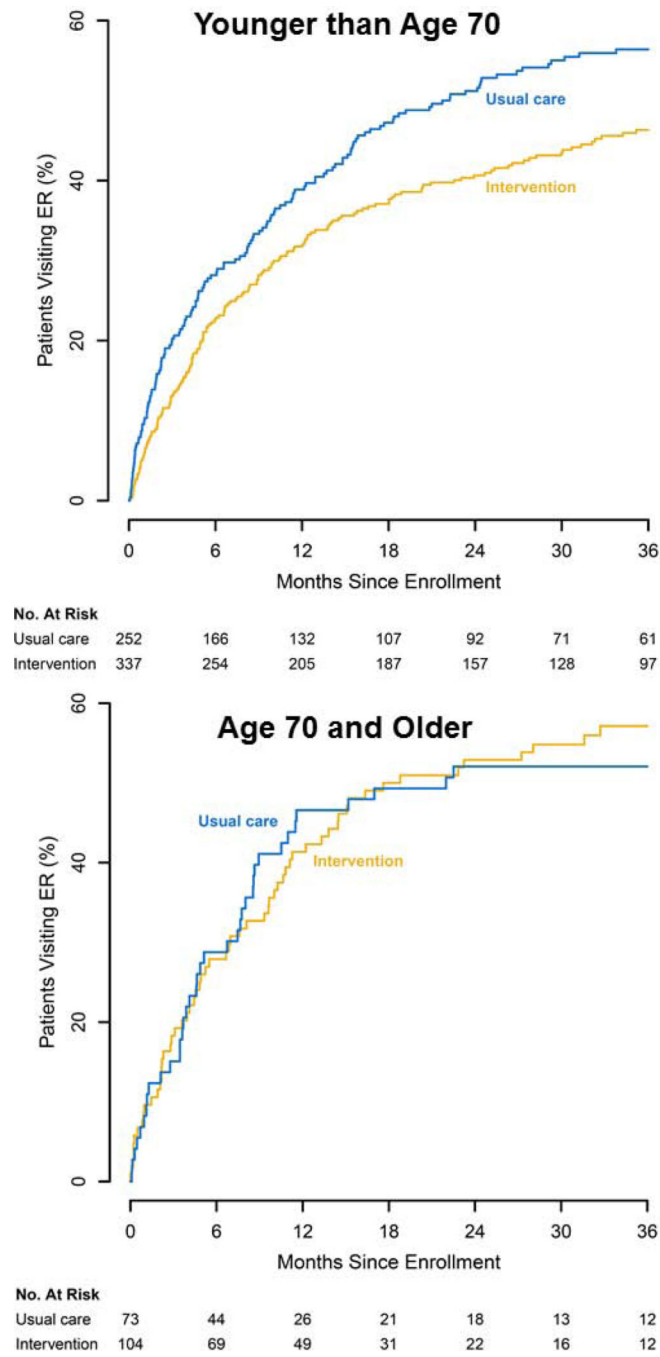


Figure 1. Effects of Electronic Patient-Reported Symptom Monitoring on ER Visits by Age
 Abbreviations: ER, emergency room; No., number.

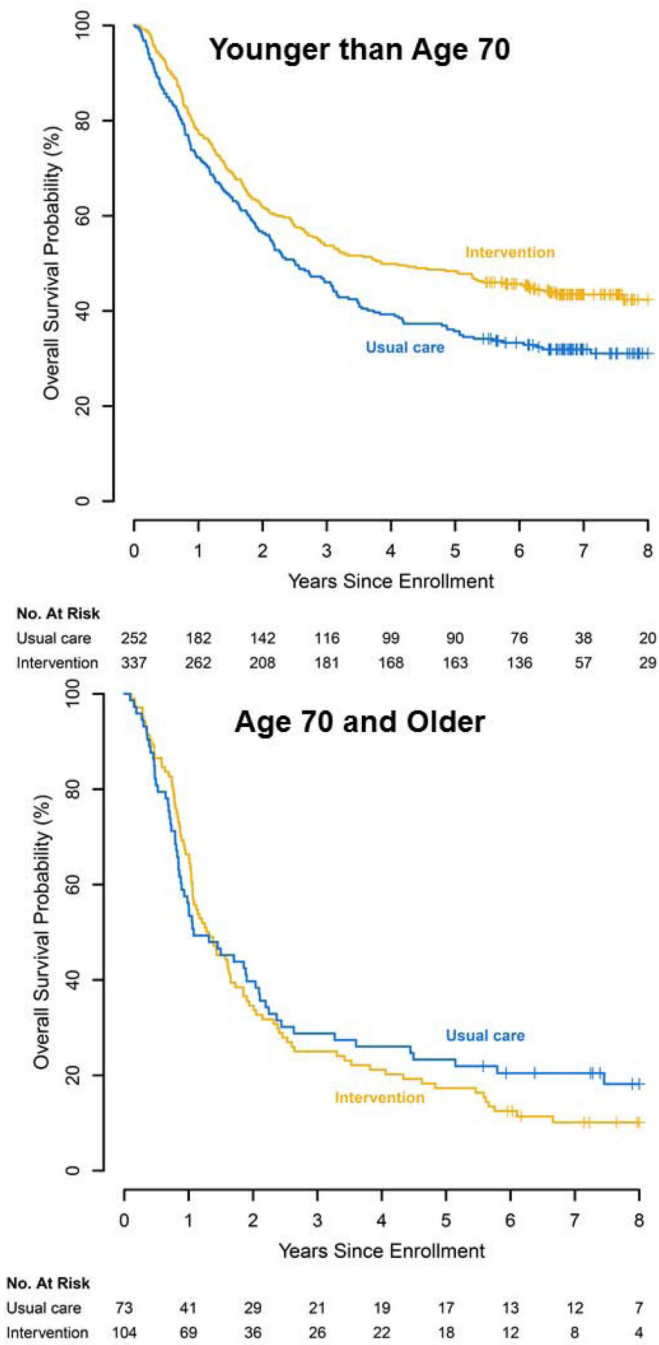


Figure 2. Effects of Electronic Patient-Reported Symptom Monitoring on Survival by Age
 Abbreviations: No., number.

Table 1.

Baseline Characteristics of Participants by Age

Characteristic	Age < 70 Years (N=589)		Age ≥ 70 Years (N=177)		P
	N	%	N	%	
Study arm					0.730
Usual Care	252	42.8	73	41.2	
Intervention	337	57.2	104	58.8	
Age					
Median (range)	58 (26 – 69)		75 (70 – 91)		
Age categories					
<50	138	23.4	-	-	
54–55	93	15.8	-	-	
55–59	99	16.8	-	-	
60–64	143	24.3	-	-	
65–69	116	19.7	-	-	
70–74	-	-	85	48.0	
75–79	-	-	56	31.6	
80+	-	-	36	20.3	
Sex					<0.001
Female	397	67.4	47	26.6	
Male	192	32.6	130	73.5	
Race					0.072
White	499	84.7	161	91.0	
Black	55	9.3	12	6.8	
Asian	35	5.9	4	2.3	
Cancer type					<0.001
Genitourinary	123	20.9	122	68.9	
Gynecologic	160	27.2	17	9.6	
Breast	140	23.8	3	1.7	
Lung	166	28.2	35	19.8	
Days since initiation of chemotherapy					0.087
Median (Range)	21 (0–840)		20 (0–1025)		
Education					0.029
High school or less	123	20.9	47	26.6	
College	292	49.6	68	38.4	
Graduate degree	174	29.5	62	35.0	
Level of prior computer experience					<0.001
Computer-Experienced	451	76.6	88	49.7	
Computer-Inexperienced	138	23.4	89	50.3	
Baseline Quality of Life					0.706
Median (range)	0.83 (0.20 to 1.00)		0.83 (0.26 to 1.00)		

Table 2. Effects of Electronic Patient-Reported Symptom Monitoring on ER Visits and Survival by Age

Outcomes*	Age < 70				Age 70			
	HR	95% CI	SE	P	HR	95% CI	SE	P
Hazard for ER Visit for Intervention vs Usual Care	0.740	0.588 to 0.933	0.118	0.011	0.895	0.581 to 1.378	0.220	0.613
Hazard for Death for Intervention vs Usual Care	0.760	0.616 to 0.938	0.107	0.011	1.056	0.751 to 1.486	0.174	0.753

Abbreviations: ER, emergency room; HR, hazard ratio; 95% CI, 95% confidence interval; SE, standard error.

* Adjusted for sex, cancer type, race, education level, and computer experience.