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Engagement with INSPIRE, an Online Program for Hematopoietic Cell Transplantation Survivors

Karen L. Syrjala [1,2,*], Marie-Laure Crouch [1], Wendy M. Leisenring [1], Mary E. D. Flowers [1,2], Samantha B. Artherholt [1,2], Allison Stover Fiscalini [1], Eleni Romano [1], Joan M. Romano [2], Paul J. Martin [1,2], Jean C. Yi [1]

[1] *Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, Washington*
[2] *Biobehavioral Sciences Department, University of Washington School of Medicine, Seattle, Washington*

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A B S T R A C T

In a secondary analysis of a randomized controlled trial (RCT), we examined participants' engagement with INSPIRE, a personalized online program for hematopoietic cell transplantation (HCT) survivors that focuses on cancer-related distress, depression, fatigue, and health care needs. We approached all adult, 3- to 18-year HCT survivors treated for hematologic malignancy without relapse or second cancer in the previous 2 years for participation in an RCT with either immediate or delayed access to INSPIRE. Participants with immediate access could view the online material at any time. Data included page view tracking, medical records, and patient-reported outcomes, including the Short Form 36 and Cancer and Treatment Distress (CTXD) measures. Of 1322 eligible HCT survivors, 771 (58%) completed the baseline assessment, and 451 received immediate INSPIRE access and were included in analyses. The cohort was 56% male, with a mean age of 52 ± 12.2 years, and 26% received an autologous transplant. Most (77%) logged into the INSPIRE site at least once, and 48% viewed ≥8 pages. Survivors who viewed ≥2 pages were more likely to be age ≥40 years (relative risk [RR], 1.41; 95% confidence interval [CI], 1.10 to 1.80), to be female (RR, 1.22; 95% CI, 1.07 to 1.40), to have chronic graft-versus-host disease (RR, 1.28; 95% CI, 1.08 to 1.51), to be less than 10 years post-HCT (RR, 1.19; 95% CI, 1.01 to 1.39), and to have moderate CTXD distress (RR, 1.34; 95% CI, 1.14 to 1.57). Engagement did not differ by race, education, income, rural/urban residence, computer experience, donor type, or depression (all $P \geq .50$). The INSPIRE online program was widely used, including by those who often have reduced access to care after treatment.

INTRODUCTION

With more than 80% of adult cancer survivors reporting using the Internet to obtain health-related information, online programs are being developed to address the chronic health and emotional problems that they may face related to late effects of treatment [1]. Hematopoietic cell transplantation (HCT) recipients have one of the highest risks of early mortality, and up to 80% have at least one chronic health condition [2-6]. Many experience isolation and long-term emotional distress, exacerbated by a lack of knowledge of HCT survivorship concerns by their post-transplantation healthcare providers [7-9].

The Internet is particularly well suited to meet the needs of this population by providing personalized educational and support materials. Online information is accessible globally on demand. With minimal moderator time, online sites also allow for oversight and input from experts. Recent clinical trials appear promising in their ability to reach targeted cancer survivors, although randomized controlled trials (RCTs) demonstrating improved outcomes in cancer survivors accessing online programs are uncommon, with limited evidence of efficacy [10-20].

The capability to enroll a targeted population (reach) and the ability to have people view and maintain use of the program (engagement) are central to the efficacy of an online program [21,22]. Although studies show that engagement declines rapidly [21,22], strategies such as sending "push" e-mail links, regularly updating content, and providing personal feedback and contact can enhance engagement [23-29]. Conversely, some studies have demonstrated that characteristics of individuals most likely to enroll in or engage with

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* Correspondence and reprint requests: Karen L. Syrjala, PhD, FHCRC, Clinical Research Division, Fred Hutchinson Cancer Research Center, 1100 Fairview Ave N, D5-220, Seattle, WA 98109.
E-mail address: ksyrjala@fredhutch.org (K.L. Syrjala).

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an online program include white race, female sex, younger age, higher income and education, and healthy, with less depression and fewer comorbidities [1,30-33].

The INSPIRE RCT (NCT00799461) was designed to assess the efficacy of a personalized Internet-based survivorship care program targeting emotional distress, depression, and fatigue compared with a delayed-access control group. We previously described the development, content, and implementation of the RCT and analyzed its reach, finding that 58% consented to the study and completed the baseline assessment [19]. Enrollment was lower for those of a nonwhite race, under age 40 years, or whose had undergone HCT ≥10 years before being approached for enrollment. The primary analysis of the RCT demonstrated that those who made use of the INSPIRE online program with companion problem-solving telehealth calls were significantly more likely than controls to improve from "distressed" to "not distressed" status (45% improved versus 20%), whereas those randomized to INSPIRE alone were marginally more likely to improve in distress (40% improved versus 20%) [34]. Supporting the value of engagement with the online program, those who viewed ≥2 pages of the online site were more likely to improve in depression or distress, consistent with findings from other online studies [35].

Here we describe patterns of engagement with INSPIRE by participants randomized to receive immediate access. Based on findings from previous online studies, we hypothesized that more site pages would be viewed by younger, white survivors with higher educational and income levels. We also hypothesized, based on previous results, that more pages would be viewed by participants with moderate, but not severe, targeted needs (ie, distress, depression, fatigue, or such health care problems as comorbidities or chronic graft-versus-host disease [cGVHD]).

MATERIALS AND METHODS

Participants

All 3- to 18-year post-HCT survivors treated for a hematologic malignancy at a single transplantation center were approached if they were age ≥18 years, resided in the United States or Canada, had experienced no relapse or second cancer in the previous 2 years, had Internet and e-mail access, and had adequate English skills to complete the baseline assessment. Consenting participants were given access to the INSPIRE site, but were not randomized if they reported potential severe depression or suicidal ideation, as indicated by a score on the Symptom Checklist-90-R of ≥3.0 or endorsement of "thoughts of ending your life" with a response of "sometimes" or more often. These participants were called by an investigator to screen for need for emergency treatment, and none required intervention. Because these individuals received immediate access to INSPIRE and represent the more severe depression continuum that is of interest for targeted online interventions, they are included in these analyses.

Procedures

All procedures were approved by the Institutional Review Board of the Fred Hutchinson Cancer Research Center. Informed consent was obtained from each participant in the study. Up to 3 letters of approach describing the study, with stamped return envelopes, were sent to potential participants, who could indicate interest or opt out. Participants also could directly access the INSPIRE URL provided in the letter to obtain study details, register through the secure patient portal, provide consent, and complete the patient-reported outcomes (PRO) baseline assessment. If a survivor did not respond, the study coordinator called to determine interest and eligibility and to facilitate enrollment. Eligible participants were randomized to either delayed INSPIRE access (after outcome assessment) or immediate INSPIRE access.

Study Internet Site and Intervention

The Internet site was developed for this study contains 5 major sections: "Boosting Health," "Restoring Energy," "Renewing Outlook," "Getting Connected," and "Tips and Tools," addressing other topics such as sleep, sexual function, and memory [19]. Content experts updated health news on a quarterly basis. Participants could submit comments and questions that were posted to the site, with responses from investigators or other participants.

Participants were sent a welcome e-mail with a link to the INSPIRE site, where they were greeted by a personalized welcome page and suggestions for pages to visit as determined by PRO scores. Participants reporting no elevated depression, distress, or fatigue scores at baseline were linked to "Boosting Health," which emphasizes personalized health care recommendations. To promote engagement, 8 e-mail pushes were sent over 3 months, first linking to areas of increased needs and then linking to other sections.

Measures

Data sources included medical records, PRO information, and automated INSPIRE page view tracking by date and time linked to the study identification code. Research medical records provided donor type, diagnosis, years post-transplantation, and history of relapse and cGVHD. Rural versus urban residence was determined from ZIP codes using the Medicare and Medicaid cms.gov categorizations.

PRO information included race, ethnicity, education and income, experience with computers (beginning, intermediate, or expert), cGVHD status, and standardized measures of quality of life and health. The Short Form 36 Health Survey (SF-36) measures physical quality of life with the Physical Component Summary (PCS) [36]. The Symptom Checklist-90-R depression scale measures 20 symptoms on a numeric scale of 0 (not at all) to 4 (extremely), with a score >1.72 indicating elevated depressive symptoms [37,38]. The Cancer and Treatment Distress scale designed for HCT recipients measures 23 potential stressors on a scale of 0 (no distress) to 3 (severe distress), with a score >1.1 indicating elevated distress [39,40]. The Fatigue Symptom Inventory contains 13 items rated on a scale of 0 (no fatigue) to 10 (extreme fatigue), with a score ≥3.0 indicating elevated fatigue [41,42]. Healthcare utilization was assessed to rate adherence to recommended surveillance [43]. Adherence to 15 health care items is converted to a percentage of recommendations adhered to. The 18-item Self-Administered Comorbidity Questionnaire parallels the medical records-based Charlson Comorbidity Index and has acceptable reliability [44]. Scores can range from 0 to 18, with a higher score indicating more comorbidities.

Statistical Analyses

Descriptive and inferential analyses were performed using the Stata 13.1 statistical software package [45]. The chi-square or Fisher exact test was used to evaluate univariate relationships between candidate factors and to categorize the number of pages viewed, as well as a binary outcome indicating INSPIRE site engagement of ≥2 (2+) pages viewed versus 0 or 1 page viewed. This required that the participant click on the site landing page and then click to at least 1 additional content page. Categories for defining engagement were determined by natural breaks in the page viewing distribution, since no research defines "sufficient engagement." The clearest breaks were at 0 or 1 page viewed versus 2+ pages viewed, and at 7 pages viewed versus ≥8 (8+) pages viewed (data not shown).

The Pearson correlation coefficient was used to evaluate pairwise correlations among variables to determine possible collinearities for multivariable analyses. Further analyses evaluated adjusted associations between candidate variables and the binary pages viewed. Generalized linear models with a log-link function, Poisson error structure, and robust variance estimates were used to directly estimate the relative risk (RR) of these associations [46]. Multivariable regression models were fit in a hierarchical manner, first identifying demographic and treatment variables that were independently associated with 2+ pages viewed. Once a multivariable model was built with those covariates, each of the PRO variables was fit one by one in this adjusted model, and ultimately a full multivariable model was built by incorporating factors with continued independent contributions to the model using step-up and step-down modeling procedures, as well as knowledge of between-factor correlations. Although factors with a P value <.10 were retained in the final multivariable models, an α value of .05 was used to determine statistical significance.

RESULTS

Characteristics of Participants Assigned to Immediate INSPIRE Site Access

Of a total of 1775 HCT survivors approached, 1346 met the screening eligibility criteria and were not lost to follow-up or deceased (Figure 1). Of these, 854 consented to participate, 59 did not complete the baseline assessment, and 24 had received cancer treatment in the previous 2 years and thus were ineligible for the study intervention. An addition-