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Article

# Receptivity to a Nurse-Led Symptom Management Intervention Among Highly Symptomatic Patients With Cancer

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## Abstract

**Background:** The symptom burden associated with cancer and its treatment can negatively affect patients' quality of life and survival. Symptom-focused collaborative care model (CCM) interventions can improve outcomes, but only if patients engage with them. We assessed the receptivity of severely symptomatic oncology patients to a remote nurse-led CCM intervention. **Methods:** In a pragmatic, cluster-randomized, stepped-wedge trial conducted as part of the National Cancer Institute IMPACT Consortium (E2C2, NCT03892967), patients receiving cancer care were asked to rate their sleep disturbance, pain, anxiety, emotional distress, fatigue, and limitations in physical function. Patients reporting at least 1 severe symptom (≥7/10) were offered phone consultation with a nurse symptom care manager (RN SCM). Initially, patients had to "opt-in" to receive a call, but the protocol was later modified so they had to "opt-out" if they did not want a call. We assessed the impact of opt-in vs opt-out framing and patient characteristics on receptiveness to RN SCM calls. All statistical tests were 2-sided. **Results:** Of the 1204 symptom assessments (from 864 patients) on which at least 1 severe symptom was documented, 469 (39.0%) indicated receptivity to an RN SCM phone call. The opt-out period (odds ratio [OR] = 1.61, 95% confidence interval [CI] = 1.12 to 2.32, $P = .01$), receiving care at a tertiary care center (OR = 3.59, 95% CI = 2.18 to 5.91, $P < .001$), and having severe pain (OR = 1.80, 95% CI = 1.24 to 2.62, $P = .002$) were associated with statistically significantly greater willingness to receive a call. **Conclusions:** Many severely symptomatic patients were not receptive to an RN SCM phone call. Better understanding of reasons for refusal and strategies for improving patient receptivity are needed.

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Cancer and its treatment cause physical, emotional, and social burdens that can negatively affect quality of life, adherence to recommended therapy, and survival (1-5). Symptom management during and following cancer therapy is often suboptimal (6,7), in part due to a lack of clinician awareness regarding how patients are feeling (8,9). Providing clinicians with patient-reported outcome measures (PROM) reports improves patient satisfaction, detection of unrecognized problems, and patient-provider communication, but alone does not improve symptom burden or quality of life (10-13). However, when PROMs are used to trigger evidence-based multidisciplinary interventions, substantial improvements in these outcomes have been demonstrated (14-18). For example, in the COPE (Collaborative Care to Preserve Performance in Cancer) trial, physical function increased, pain scores decreased, and health-care use decreased among patients with advanced cancer when PROM scores triggered physical therapist-led telerehabilitation (19). These benefits were not observed with PROM score reporting alone. Collaborative care model (CCM)-based interventions are evidence-based approaches wherein patient-reported symptoms are monitored and managed by a team of providers (usually nurses or other care managers in addition to physicians)

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with complementary areas of expertise. CCM interventions have shown promise for symptom management in a variety of clinical contexts, including cancer clinics (20-24). For instance, in a UK study, patients with recently treated lung cancer who received monthly nurse telephone calls or visits in a nurse-led clinic in addition to routine care reported less severe dyspnea at 3 months and fewer emotional difficulties and peripheral neuropathy at 3 months (25).

The Enhanced, EHR-facilitated Cancer Symptom Control (E2C2, NCT03892967) trial is currently underway as part of the National Cancer Institute's Improving the Management of symPtoms during And following Cancer Treatment (IMPACT) Consortium (https://healthcaredelivery.cancer.gov/impact/). The goal of the IMPACT Consortium is to improve symptom control for patients with cancer. Research centers are testing systems that engage patients in systematic symptom reporting and guideline-based clinical management and evaluating the effects on patient-centered outcomes . E2C2 assesses the effect of a CCM-based intervention (including phone calls from registered nurse symptom care managers [RN SCMs])—triggered by electronic health record (EHR)–administered PROMs—on sleep, pain, anxiety, emotional distress or depression, and fatigue (SPADE) symptoms and limitations in physical function among patients with cancer (26).

The effectiveness of any CCM intervention depends, in part, on patient willingness to engage with it. Pragmatic data regarding patient receptivity to CCM interventions are limited because most trials investigating such interventions use an automatic enrollment strategy. In this interim analysis of the E2C2 trial, we sought to investigate the willingness of patients with 1 or more severe symptom(s) and/or a limitation in physical function to engage with RN SCM phone calls. Specifically, we evaluated the effect of an opt-in vs opt-out framing strategy; demographic, clinical, and symptom characteristics; and the COVID-19 pandemic.

The impact of transitioning from an opt-in to opt-out strategy was of particular interest, because opt-out strategies have been shown to be superior for intervention receptivity in other study contexts. For example, for poorly controlled diabetic patients in primary care practices, recruitment into a behavioral intervention trial was statistically significantly increased by opt-out compared with opt-in framing (38% vs 13%, $P < .001$) (27). Other instances where opt-out strategies have increased uptake of an intervention include HIV screening, colorectal cancer screening, and organ donation (28-30).

## Methods

### E2C2 Parent Trial Design

The E2C2 trial is an ongoing, pragmatic, group-randomized, stepped-wedge trial enrolling adults receiving care for solid tumors at Mayo Clinic Rochester (MCR) or solid and liquid tumors at a community site in the Midwest Mayo Clinic Health System (MCHS) (26). Clusters were determined by disease type for patients at MCR and by location for patients in the MCHS. Three clusters were randomly assigned to each of 5 steps; these steps enter the intervention condition at staggered 8-month intervals. The current analysis included data from the clusters in the first 2 steps. The 3 clusters in step 1 were 1) patients with genitourinary cancer seen at MCR, 2) patients with head and neck malignancy seen at MCR, and 3) patients with any form of cancer treated at the LaCrosse, Wisconsin, MCHS community site. The clusters in step 2 were 1) patients seen at MCR with sarcoma, 2) patients seen at MCR with lung cancer, and 3) one-half of the patients seen at MCR for gastrointestinal malignancy. Patients were included regardless of cancer stage or treatment status.

The primary instrument used to collect PROMs is a 6-item "Brief Symptom and Function Screen" (BSFS), which asks patients to report the severity of sleep disturbance, pain, anxiety, emotional distress (as a surrogate for depression), fatigue, and limitations in physical function over the last 7 days. These domains are graded on a scale from 0 (no symptoms) to 10 (as bad as could be imagined). Patients reporting a score of 7 or greater on 1 or more of the SPADE symptoms or limitations in physical function are considered to have severe symptom burden (31,32). This questionnaire was patterned on similar linear analog scales that have been validated for symptom assessment in patients with cancer (31,33). Patients are asked to complete the BSFS questionnaire in their EHR patient portal 4 days before each medical oncology clinic appointment. If not completed before the visit, patients are prompted to complete the BSFS on a tablet in the clinic waiting room. Alternatively, clinic staff may also administer the questionnaire and manually enter patients' responses into the EHR. The BSFS is not administered more frequently than every 14 days. Although between-visit assessments were initiated in July 2020, this article reports only on data derived from completed questionnaires that were linked to a clinic visit (in-person or virtual).

Data collected through August 28, 2020, were included in our analysis. The parent E2C2 trial data collection will continue recruitment through January 31, 2023.

The E2C2 protocol was approved by the Mayo institutional review board as exempt research not requiring informed consent. As such, no approvals or consents by patients or clinicians were sought before survey administration.

### CCM Intervention

On October 1, 2019, the clusters randomly assigned to step 1 started to receive the E2C2 CCM intervention. The clusters randomly assigned to step 2 began receiving the CCM intervention on June 1, 2020 (Figure 1). As part of this intervention, patients with 1 or more severe symptom scores are offered educational materials (available in both electronic and printed formats), access to an online community of patients with cancer-related symptoms, and an algorithm-guided phone call from an RN SCM. The intent of the call is to encourage self-management of symptoms, provide symptom-specific medication management, and offer specialist referrals (if necessary). All nurses involved with making the RN SCM phone calls are RNs who have completed human patients in research training. When a severe symptom is reported, a patient is shown several sentences describing the RN SCM as a symptom specialist who will work with their care team to help manage their symptoms if desired.

### Variables and Trial Framing

Receptivity among patients with severe symptom burden to an RN SCM phone call was the primary outcome of interest in the current analysis. During the opt-in period, participants with 1+ severe symptom(s) were shown the following text: "Patients often find it helpful to speak with a nurse specialist about severe symptoms. Please indicate all symptoms you would like to

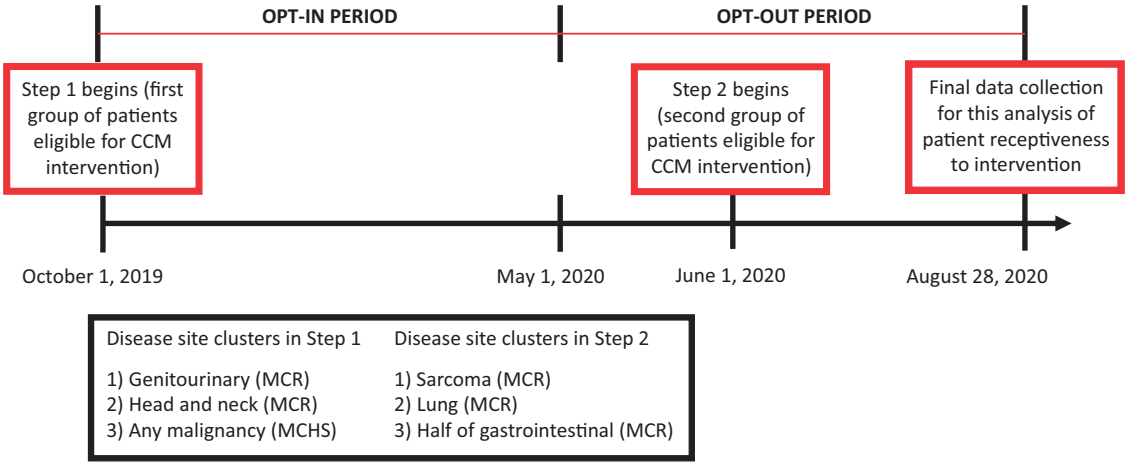


**Figure 1.** Timeline for data collection related to analysis of patient receptivity to CCM intervention. The timeline in the figure is not to scale. CCM = collaborative care model; MCHS = Mayo Clinic Health System; MCR = Mayo Clinic Rochester.

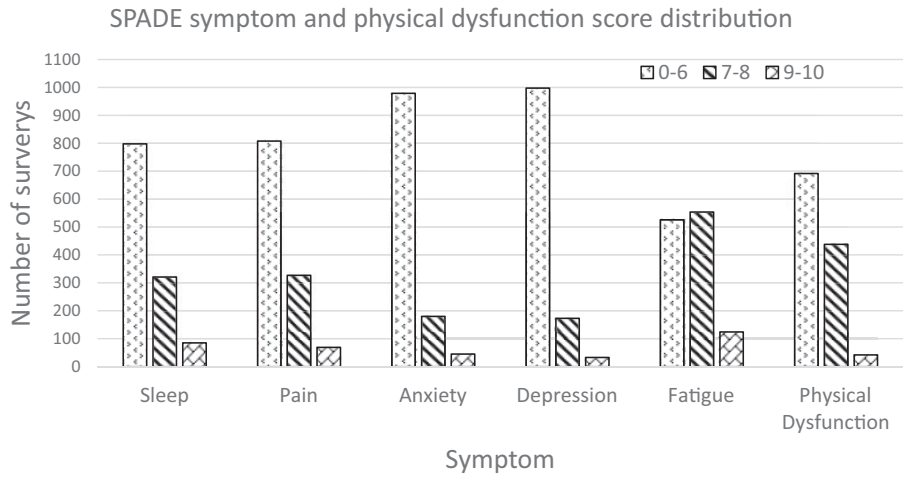


**Figure 2.** Distribution of non-severe (<7), severe (7-8) and very severe (9-10) symptom scores from surveys collected during the trail (both opt-in and opt-out periods).

discuss with a nurse. Select all that apply." Response options were as follows: "limitations with physical function," "trouble sleeping," "emotional distress, feeling depressed," "anxiety," "pain," "fatigue," "nothing at this time," and "already working with SCM." In contrast, in the opt-out period (starting May 1, 2020), this text was changed to "We recommend that you speak with a nurse symptom care manager. This is a nurse who specializes in helping you manage your symptoms and works closely with your oncology care team." Patients then had an option to "continue" or click "I do not want help with my symptoms at this time." During the opt-in period, patients were considered to be receptive only if they selected 1 or more symptoms that they wanted to discuss with a nurse. During the opt-out period, patients were considered receptive if they did not decline help.

Independent variables included whether the patient completed the questionnaire during the opt-in vs the opt-out period, cancer type, demographic factors (age and sex), SPADE and limitation in physical function scores (discretized as $<7$ vs $\geq 7$, and in secondary analyses, as 0-6 for "not severe," 7-8 for "less severe," and 9-10 for "very severe"), number of concurrent severe scores, and care site (tertiary care vs community site).

Because of changes in practice patterns across the health system as well as in patient preferences for care delivery with the onset of the COVID-19 pandemic, we also compared the pre-COVID (October 1, 2019-March 15, 2020) vs COVID (March 15-April 30, 2020) phase of the opt-in period.

## Statistical Analysis

Descriptive statistics (counts, frequencies, percentages) were used to summarize participants' demographic and clinical characteristics. Symptom scores and receptivity to an RN SCM phone call were summarized for the total sample first, and then the sample was stratified by framing period (opt-in vs opt-out). Because patients could have completed multiple questionnaires in 1 or both periods, we summarized characteristics by questionnaire rather than by patient. We first estimated a set of bivariate models, 1 for each factor (age, sex, cancer type, hospital, SPADE symptom, limitation in physical function, number of severe scores), with receptivity to the RN SCM phone call as the dependent variable. For each effect, we reported the odds ratio (OR) and 95% confidence interval (CI). Then, to test whether opt-

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**Table 1.** Characteristics of questionnaire respondents, as well as their openness to a RN SCM phone call, by questionnaire (only including those with a least 1 severe symptom reported), stratified by trial period[a]

| Characteristic | Opt-in period, No. (%) | Opt-out period, No. (%) | All, No. (%) |
|---|---|---|---|
| Total | 540 (100.0) | 664 (100.0) | 1204 (100.0) |
| Age, y | | | |
| 18-55 | 102 (18.9) | 139 (20.9) | 241 (20.0) |
| 56-65 | 168 (31.1) | 197 (29.7) | 365 (30.3) |
| 66-75 | 176 (32.6) | 205 (30.9) | 381 (31.6) |
| 76-80 | 52 (9.6) | 69 (10.4) | 121 (10.0) |
| 80+ | 41 (7.6) | 54 (8.1) | 95 (7.9) |
| Missing | 1 (0.2) | 0 (0.0) | 1 (0.1) |
| Sex | | | |
| Female | 224 (41.5) | 297 (44.7) | 521 (43.3) |
| Male | 315 (58.3) | 367 (55.3) | 682 (56.6) |
| Missing | 1 (0.2) | 0 (0.0) | 1 (0.1) |
| Cancer type | | | |
| GU | 166 (30.7) | 74 (11.1) | 240 (19.9) |
| Breast | 49 (9.1) | 23 (3.5) | 72 (6.0) |
| Endo | 6 (1.1) | 5 (0.8) | 11 (0.9) |
| GI | 32 (5.9) | 123 (18.5) | 155 (12.9) |
| Gyn | 8 (1.5) | 7 (1.1) | 15 (1.2) |
| Head and neck | 124 (23.0) | 54 (8.1) | 178 (14.8) |
| Heme | 27 (5.0) | 18 (2.7) | 45 (3.7) |
| Lung | 39 (7.2) | 239 (36.0) | 278 (23.1) |
| Melanoma | 8 (1.5) | 3 (0.5) | 11 (0.9) |
| Other | 52 (9.6) | 45 (6.8) | 97 (8.1) |
| Sarcoma | 29 (5.4) | 73 (11.0) | 102 (8.5) |
| Site | | | |
| Community | 209 (38.7) | 132 (19.9) | 341 (28.3) |
| Tertiary care | 331 (61.3) | 532 (80.1) | 863 (71.7) |
| Sleep score | | | |
| 0-6 | 359 (66.5) | 439 (66.1) | 798 (66.3) |
| 7-8 | 143 (26.5) | 178 (26.8) | 321 (26.7) |
| 9-10 | 38 (7.0) | 47 (7.1) | 85 (7.1) |
| Pain score | | | |
| 0-6 | 366 (67.8) | 442 (66.6) | 808 (67.1) |
| 7-8 | 147 (27.2) | 180 (27.1) | 327 (27.2) |
| 9-10 | 27 (5.0) | 42 (6.3) | 69 (5.7) |
| Anxiety score | | | |
| 0-6 | 444 (82.2) | 535 (80.6) | 979 (81.3) |
| 7-8 | 78 (14.4) | 102 (15.4) | 180 (15.0) |
| 9-10 | 18 (3.3) | 27 (4.1) | 45 (3.7) |
| Depression score | | | |
| 0-6 | 446 (82.6) | 552 (83.1) | 998 (82.9) |
| 7-8 | 81 (15.0) | 92 (13.9) | 173 (14.4) |
| 9-10 | 13 (2.4) | 20 (3.0) | 33 (2.7) |
| Fatigue score | | | |
| 0-6 | 257 (47.6) | 269 (40.5) | 526 (43.7) |
| 7-8 | 230 (42.6) | 324 (48.8) | 554 (46.0) |
| 9-10 | 53 (9.8) | 71 (10.7) | 124 (10.3) |
| Limitation in physical function score | | | |
| 0-6 | 304 (56.3) | 388 (58.4) | 692 (57.5) |
| 7-8 | 194 (35.9) | 244 (36.7) | 438 (36.4) |
| 9-10 | 42 (7.8) | 32 (4.8) | 74 (6.1) |
| No. of severe scores | | | |
| 1 | 251 (46.5) | 286 (43.1) | 537 (44.6) |
| 2 | 156 (28.9) | 190 (28.6) | 346 (28.7) |
| 3 | 71 (13.1) | 104 (15.7) | 175 (14.5) |
| 4 | 34 (6.3) | 51 (7.7) | 85 (7.1) |
| 5 | 16 (3.0) | 21 (3.2) | 37 (3.1) |
| 6 | 12 (2.2) | 12 (1.8) | 24 (2.0) |
| Receptive to RN SCM call | | | |
| No | 369 (68.3) | 366 (55.1) | 735 (61.0) |
| Yes | 171 (31.7) | 298 (44.9) | 469 (39.0) |

[a] Scores for sleep, pain, anxiety, depression, fatigue, and limitation in physical function are based on self-report on a linear analogue scale from 0-10. Endo = endocrine; GI = gastrointenstinal; GU = genitourinary; Gyn = gynecologic; Heme = hematologic; RN SCM = nurse symptom care manager.

**Table 2.** Univariate and multivariable analysis of demographic factors, cancer type, symptoms, and opt-in vs opt-out design that predict receptivity to an RN SCM phone call

| Characteristic | Bivariate OR (95% CI) | P | Multivariable OR (95% CI) | P |
|---|---|---|---|---|
| Period | | <.001[a] | | .01[a] |
| Opt-in | Ref | | Ref | |
| Opt-out | 2.09 (1.51 to 2.90) | | 1.61 (1.12 to 2.32) | |
| Age, y | | .43[a] | | .76[a] |
| 18-55 | Ref | | Ref | |
| 56-65 | 1.16 (0.73 to 1.83) | .53[b] | 1.18 (0.75 to 1.86) | .48[b] |
| 66-75 | 0.83 (0.53 to 1.31) | .43[b] | 0.97 (0.61 to 1.53) | .89[b] |
| 76-80 | 0.79 (0.43 to 1.44) | .44[b] | 0.86 (0.46 to 1.60) | .63[b] |
| 80+ | 0.76 (0.39 to 1.47) | .41[b] | 0.86 (0.44 to 1.70) | .48[b] |
| Sex | | .34[a] | | .69[a] |
| Female | Ref | | Ref | |
| Male | 1.17 (0.85 to 1.62) | | 0.93 (0.65 to 1.33) | |
| Cancer type | | .002[a] | | .81[a] |
| GU | Ref | | Ref | |
| Breast | 0.40 (0.18 to 0.86) | .02[b] | 1.05 (0.43 to 2.61) | .91[b] |
| Endo | 0.29 (0.04 to 1.87) | .19[b] | 0.38 (0.06 to 2.44) | .31[b] |
| GI | 1.12 (0.65 to 1.94) | .67[b] | 1.04 (0.57 to 1.90) | .89[b] |
| Gyn | 0.16 (0.03 to 1.02) | .05[b] | 0.32 (0.05 to 2.10) | .23[b] |
| Head and neck | 1.00 (0.59 to 1.72) | .99[b] | 0.85 (0.50 to 1.46) | .56[b] |
| Heme | 0.23 (0.08 to 0.64) | .005[b] | 0.64 (0.21 to 1.94) | .43[b] |
| Lung | 1.35 (0.85 to 2.16) | .21[b] | 0.96 (0.57 to 1.61) | .87[b] |
| Melanoma | 0.27 (0.04 to 1.88) | .19[b] | 0.38 (0.05 to 2.71) | .33[b] |
| Other | 0.61 (0.32 to 1.17) | .14[b] | 0.77 (0.39 to 1.52) | .45[b] |
| Sarcoma | 0.66 (0.35 to 1.26) | .21[b] | 0.65 (0.32 to 1.30) | .23[b] |
| Site | | <.001[a] | | <.001[a] |
| Community | Ref | | Ref | |
| Tertiary care | 4.28 (2.86 to 6.41) | | 3.59 (2.18 to 5.91) | |
| Sleep score | | .09[a] | | .03[a] |
| <7 | Ref | | Ref | |
| 7+ | 1.33 (0.96 to 1.83) | | 1.52 (1.05 to 2.20) | |
| Pain score | | .006[a] | | .002[a] |
| <7 | Ref | | Ref | |
| 7+ | 1.58 (1.14 to 2.19) | | 1.80 (1.24 to 2.62) | |
| Anxiety score | | .07[a] | | .06[a] |
| <7 | Ref | | Ref | |
| 7+ | 1.44 (0.97 to 2.13) | | 1.62 (0.98 to 2.67) | |
| Depression score | | .44[a] | | .79[a] |
| <7 | Ref | | Ref | |
| 7+ | 1.17 (0.79 to 1.74) | | 1.07 (0.64 to 1.79) | |
| Fatigue score | | .09[a] | | .03[a] |
| <7 | Ref | | Ref | |
| 7+ | 1.32 (0.96 to 1.81) | | 1.54 (1.05 to 2.24) | |
| Limitation in physical function score | | .28[a] | | .49[a] |
| <7 | Ref | | Ref | |
| 7+ | 0.84 (0.62 to 1.15) | | 0.88 (0.61 to 1.27) | |
| No. of severe scores | | .03[a] | | .24[a] |
| 1 | Ref | | Ref | |
| 2 | 1.29 (0.90 to 1.84) | .16[b] | 0.99 (0.67 to 1.47) | .95[b] |
| 3 | 1.47 (0.94 to 2.30) | .10[b] | 0.73 (0.40 to 1.31) | .29[b] |
| 4 | 1.02 (0.55 to 1.90) | .95[b] | 0.40 (0.17 to 0.94) | .04[b] |
| 5 | 2.16 (0.91 to 5.13) | .08[b] | 0.59 (0.18 to 1.88) | .37 [b] |
| 6 | 5.22 (1.71 to 15.89) | .004[b] | [c] | |

[a]P values for each categorical variable calculated using a 2-sided Wald test. Endo = endocrine; GU = genitourinary; GI = gastrointestinal; Gyn = gynecologic; Heme = hematologic; RN SCM = nurse symptom care manager.
[b]Individual P values calculated using 2-sided t tests.
[c]Omitted due to collinearity.

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**Table 3.** Impact of SPADE symptom and limitation in physical function on receptivity to an RN SCM phone call, stratified by severe (7–8) and very severe (9–10) symptom scores[a]

| Symptom | Bivariate OR (95% CI) | P | Multivariable OR (95% CI) | P |
|---|---|---|---|---|
| Sleep | | .01[b] | | .02[b] |
| 0-6 | Ref | | Ref | |
| 7-8 | 1.13 (0.80 to 1.59) | .50[c] | 1.27 (0.86 to 1.89) | .23[c] |
| 9-10 | 2.44 (1.35 to 4.41) | .003[c] | 2.52 (1.33 to 4.78) | .005[c] |
| Pain | | .02[b] | | .01[b] |
| 0-6 | Ref | | Ref | |
| 7-8 | 1.59 (1.13 to 2.25) | .008[c] | 1.79 (1.21 to 2.65) | .004[c] |
| 9-10 | 1.52 (0.80 to 2.88) | .20[c] | 1.17 (0.58 to 2.37) | .67[c] |
| Anxiety | | .18[b] | | .19[b] |
| 0-6 | Ref | | Ref | |
| 7-8 | 1.39 (0.91 to 2.13) | .13[c] | 1.57 (0.94 to 2.64) | .09[c] |
| 9-10 | 1.65 (0.75 to 3.64) | .22[c] | 0.81 (0.28 to 2.34) | .86[c] |
| Depression | | .17[b] | | .21[b] |
| 0-6 | Ref | | Ref | |
| 7-8 | 1.02 (0.66 to 1.56) | .94[c] | 0.96 (0.56 to 1.63) | .87[c] |
| 9-10 | 2.39 (0.96 to 5.92) | .06[c] | 2.94 (0.85 to 10.24) | .09[c] |
| Fatigue | | .13[b] | | .17[b] |
| 0-6 | Ref | | Ref | |
| 7-8 | 1.26 (0.90 to 1.74) | .17[c] | 1.45 (0.98 to 2.13) | .06[c] |
| 9-10 | 1.67 (0.98 to 2.84) | .06[c] | 1.42 (0.80 to 2.52) | .23[c] |
| Limitation in physical function | | .16[b] | | .33[b] |
| 0-6 | Ref | | Ref | |
| 7-8 | 0.78 (0.56 to 1.08) | .14[c] | 0.78 (0.53 to 1.15) | .22[c] |
| 9-10 | 1.33 (0.71 to 2.49) | .38[c] | 1.16 (0.58 to 2.35) | .68[c] |

[a]Odds ratios (ORs) for other covariates not reported. CI = confidence interval; RN SCM = nurse symptom care manager; SPADE = sleep, pain, anxiety, emotional distress or depression, and fatigue.
[b]P values for each categorical variable calculated using a 2-sided Wald test.
[c]Individual P values calculated using 2-sided t tests.

in vs opt-out framing or other patient factors were independently associated with receptivity to a RN SCM phone call, we estimated a single multivariable model including a variable for opt-in vs opt-out, controlling for covariates. In our secondary analysis, we replicated the full set of multivariable, covariate-adjusted models but incorporated the SPADE and limitation in physical function scores as 3 ordinal categories (score 0-6, 7-8, and 9-10). In all analyses, we used a random effects model to account for the within-participant correlation of outcomes over time.

We performed a secondary analysis to assess whether interruptions in care related to COVID-19 influenced our findings. We replicated the primary models using the trinary independent variable, which separated opt-in questionnaires into pre-COVID and COVID phases.

All analyses were performed using Stata 16.1 (StataCorp, College Station, TX). We used a threshold of P less than .05 to determine statistical significance; all tests were 2-sided.

## Results

Between October 1, 2019, and August 28, 2020, 11 382 questionnaires were sent to patients assigned to the first 2 steps of the E2C2 trial; 4841 questionnaires were sent during the opt-in period (October 1, 2019-April 30, 2020) and 6541 during the opt-out period (May 1, 2020-August 28, 2020). The total number of completed questionnaires were 2617 and 3514 (54% completion rate in both periods) from 1464 and 2386 unique patients, respectively. At least 1 severe symptom (score ≥7) was reported on 19.6% (1204) of the 6131 completed questionnaires. These questionnaires came from 864 unique patients (see Supplementary Table 1, available online, for questionnaires returned per patient). Characteristics of questionnaire respondents, stratified by exposure period, are reported in Table 1.

A total of 469 (39.0%) of the 1204 questionnaires with at least 1 severe symptom score indicated receptivity to an RN SCM phone call. Severely symptomatic respondents were less receptive to an RN SCM phone call if they had to opt-in rather than opt-out (31.7% vs 44.9%), as reported in Table 1. Only 137 total patients reported at least 1 severe symptom on more than 1 survey during either the opt-in or opt-out period (or both), with slightly less receptivity to the RN SCM on the second questionnaire within the period (36.6% vs 31.0% for their first vs second survey in the opt-in period, and 50.7% vs 43.8%, respectively, in the opt-out period; data not shown). Because 2 of the first 3 clusters to be offered the opportunity to opt-in to the CCM intervention were patients with genitourinary and head and neck cancers, the majority of the questionnaires (53.7%) during the opt-in time period (October 1, 2019-April 30, 2020) came from patients with these diagnoses. Lung cancer was the most common diagnosis both during the opt-out time period (36.0%) and in the total sample (23.1%). A smaller proportion of questionnaires captured in the opt-in compared with the opt-out period were from patients being seen at the tertiary care center (61.3% vs 80.1%); this is because all patients randomly assigned to step 2 were from the tertiary care center, and step 2 patients did not become eligible for the intervention until after opt-out framing started.

Across the entire data collection, the most prevalent severe symptom was fatigue, reported on more than one-half (56.3%)

of the questionnaires on which 1 or more severe symptoms were reported (Table 1). Severe anxiety (18.7%) and severe depression (17.1%) were the least common. For all symptoms and limitations in physical function, scores of 9 or 10 occurred infrequently. Most questionnaires had only 1 (44.6%) or 2 (28.7%) severe symptoms reported (Table 1; Figure 2).

Table 2 reports the impact of demographic, disease, and symptom variables on patient receptivity to an RN SCM phone call. The left column presents a bivariate analysis and the right presents a multivariable analysis. In the bivariate model, having breast cancer (OR = 0.40, 95% CI = 0.18 to 0.86, $P = .02$) or a hematologic malignancy (OR = 0.23, 95% CI = 0.08 to 0.64, $P = .005$) statistically significantly decreased patient receptivity to an RN SCM phone call ($P = .002$), whereas reporting 6 severe symptoms increased it (OR = 5.22, 95% CI = 1.71 to 15.89, $P = .004$). These associations did not retain statistical significance in the multivariable analysis.

In the covariate-adjusted multivariable analysis (shown in Table 2), 3 factors were independently associated with receptivity to an RN SCM phone call: completing the questionnaire during the opt-out period (OR = 1.61, 95% CI = 1.12 to 2.32, $P = .01$), receiving care at a tertiary care center (OR = 3.59, 95% CI = 2.18 to 5.91, $P < .001$), and having severe pain (OR = 1.80, 95% CI = 1.24 to 2.62, $P = .002$).

Table 3 presents the associations between very severe (range = 9-10), less severe (range = 7-8), and nonsevere (range = 0-6) scores and receptivity to an RN SCM phone call. In fully adjusted models, patients with severe pain scores (OR = 1.79, CI = 1.21 to 2.65, $P = .004$), but not those with very severe pain scores (OR = 1.17, 95% CI = 0.58 to 2.37, $P = .67$), were statistically significantly more likely to be receptive to RN SCM calls. The opposite was true for those with very severe (OR = 2.52, CI = 1.33 to 4.78, $P = .005$) vs severe sleep problems (OR = 1.27, 95% CI = 0.86 to 1.89, $P = .23$).

In a secondary analysis, we found that the COVID-19 pandemic was not associated with receptivity to an RN SCM phone call (Table 3). This was true in both the bivariate (OR = 1.06, 95% CI = 0.56 to 2.01) and multivariable (OR = 1.12, 95% CI = 0.59 to 2.14) analyses.

## Discussion

We examined the receptivity of a diverse group of highly symptomatic cancer patients to RN SCM phone calls. Having to opt-out (rather than opt-in), being seen at a tertiary care center, and having severe pain increased patient receptivity.

In both periods of the study, only approximately one-third of participants were receptive to calls (opted-in or did not opt-out). This is concerning because the interventions being tested in the parent E2C2 trial can only be effective if they reach the patients in need. Our receptivity rates are consistent with the findings of another study by our group in which only 32% of patients with stage IIIB or IV non-small cell or extensive stage small cell lung cancer were willing to receive physical rehabilitation services despite having statistically significant disability. In that study, commonly cited reasons for declining rehabilitation services included being too busy; thinking that rehabilitation was unnecessary, not beneficial, or too burdensome; and believing that something needed to be completed prior (eg, chemotherapy) (34). All of these concerns may have contributed to the observations we report here. Additionally, in this study, the timing of questionnaire administration just before clinic visits may have also played a role because patients may prefer to discuss symptoms in person with clinicians whom they already know when an appointment is imminent. The clinical, demographic, attitudinal, and contextual factors that may influence receptivity deserve further study, particularly since notably higher rates of receptivity to receive follow-up phone calls (84%) were reported in another study of routine symptom surveillance and intervention during breast cancer treatment (35).

Receiving care at a tertiary care site was independently associated with an increased receptivity to RN SCM phone calls. Tertiary medical centers tend to see more geographically diverse patients; these patients may be further along in their disease course or have more advanced disease, though for this interim analysis, we did not have access to stage and diagnosis date data to confirm this.

Pain was also strongly linked to increased receptivity to a RN SCM phone call, although this association was not found in those with very severe scores. Given the small number of patients reporting very severe pain, the analysis may have been statistically underpowered to detect a difference. However, it is also possible that those who are in extreme pain are less inclined to engage with clinicians by phone. Alternative intervention strategies may be more appealing to these patients (eg, in-person visits with palliative care providers). Conversely, those with very severe pain may have already been identified to receive interventions, reducing their self-perceived benefit of an RN SCM phone call.

Notably, patients with very severe sleep dysfunction (scores = 9-10) were statistically significantly more willing to receive nursing phone calls, and compared with those with scores of 7-8, severe sleep dysfunction was a statistically significant predictor of receptivity to receive an RN SCM phone call in our multivariable model (Table 2).

Sex, age, cancer type, and number of concurrent severe symptom scores had no impact on patient receptivity to the RN SCM phone calls, with the exception that patients reporting 4 concurrent severe scores appeared to be less receptive to RN SCM phone calls than those reporting 1 severe score. The reason for this is unknown. Last, changes in care delivery patterns resulting from the COVID-19 pandemic did not appear to influence patient receptivity to RN SCM symptom-focused calls.

It is worth noting that being receptive to a phone call does not guarantee that a patient will answer the phone and engage with an RN SCM. Thus, the number of patients who ultimately receive the intervention may be substantially lower. The proportion of patients who actually engage with the RN SCM will be reported with full study results.

A salient strength of this analysis is the size and diversity of our sample. However, although this heterogeneity improves generalizability, it may also obscure findings that are specific to certain settings or populations (eg, patients initiating first-line chemotherapy). Another caveat is that several variables that may affect openness to the CCM intervention were not available for interim analysis, including race or ethnicity, cancer stage, and place along the cancer care continuum. Moreover, we were unable to ascertain the degree to which cancer care teams endorsed the intervention to their patients, Additionally, our definitions of symptom severity (which were linked to eligibility for an RN SCM phone call) were based on expert clinical judgment and on literature suggesting that fatigue and pain scores greater than or equal to 7 on 0-10 scales indicate severe burden. It is possible that patient receptivity to RN SCM phone calls would have been different if we had used another score threshold. Last, because the change from opt-in to opt-out was made at a single point in time, there is the possibility of time-modified

confounding. Next steps include qualitative interviews to investigate patient perceptions of the symptom management intervention and to identify reasons underlying low receptivity and potential impediments to engagement.

The use of EHR-administered PROMs to identify and offer a CCM intervention to highly symptomatic patients will only be effective if patients are receptive to the intervention. Certain patients may be unwilling to do so, despite having severe symptoms. Empiric evidence to support the selection of strategies for engaging patients with symptom-focused interventions is needed.

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## Data Availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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